Devi, S.
09/715876

-key terms

FILE 'HCAPLUS' ENTERED AT 09:48:00 ON 07 OCT 2002)
L1 3402 SEA FILE=HCAPLUS ABB=ON PLU=ON ALS1? OR ALSI? OR ALS(S)AGGLUTIN? OR AGGLUTIN?(W)LIKE
L2 23 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 AND (CANDIDA OR ALBICANS OR KRUSEI OR TROPICALIS OR PARAPSILOS?)

L2 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:712015 HCAPLUS
TITLE: Adhesion in **Candida** spp
AUTHOR(S): Sundstrom, Paula
CORPORATE SOURCE: Department of Molecular Virology, Immunology and Medical Genetics, and the Department of Microbiology, The Ohio State University College of Medicine, Columbus, OH, 43210-1239, USA
SOURCE: Cellular Microbiology (2002), 4(8), 461-469
CODEN: CEMIF5; ISSN: 1462-5814
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Microbial adherence is one of the most important determinants of pathogenesis, yet very few adhesins have been identified from fungal pathogens. Four structurally related adhesins, Hwp1, Ala1p/Als5p, **Als1p**, from **Candida albicans** and Epa1p from **Candida** glabrata, are members of a class of proteins termed glycosylphosphatidylinositol-dependent cell wall proteins (GPI-CWP). These proteins have N-terminal signal peptides and C-terminal features that mediate glycosylphosphatidylinositol (GPI) membrane anchor addn., as well as other determinants leading to attachment to cell wall glucan. While common signalP/GPI motifs facilitate cell surface expression, unique features mediate ligand binding specificities of adhesins. The first glimpse of structural features of putative adhesins has come from biophys. characterizations of the N-terminal domain of Als5p. One protein not in the GPI-CWP class that was initially described as an adhesin, Int1p, has recently been shown to be similar to Bud4p of Saccharomyces cerevisiae in primary amino acid sequence, in co-localizing with septins and in functioning in bud site selection. Progress in understanding the role of adhesins in oroesophageal candidiasis has been made for Hwp1 in a study using beige athymic and transgenic .epsilon.26 mice that have combined defects in innate and acquired immune responses. Searches of the C. **albicans** genome for proteins in the GPI-CWP class has led to the identification of a subset of genes that will be the focus of future efforts to identify new **Candida** adhesins.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:639230 HCAPLUS
TITLE: Contribution of **Candida albicans ALS1** to the pathogenesis of experimental oropharyngeal candidiasis
AUTHOR(S): Kamai, Yasuki; Kubota, Mikie; Kamai, Yoko; Hosokawa, Tsunemichi; Fukuoka, Takashi; Filler, Scott G.
CORPORATE SOURCE: Biological Research Laboratories, Sankyo Co.,

Ltd., Tokyo, 140-8710, Japan
SOURCE: Infection and Immunity (2002), 70(9), 5256-5258
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We investigated the contribution of **Candida albicans ALS1**, which encodes a candidal adhesin, to the pathogenesis of exptl. murine oropharyngeal candidiasis. Our results indicate that the **ALS1** gene product is important for the adherence of the organism to the oral mucosa during the early stage of the infection.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:355852 HCAPLUS
DOCUMENT NUMBER: 137:90678
TITLE: **Candida albicans Als1p**: An adhesin that is a downstream effector of the EFG1 filamentation pathway
AUTHOR(S): Fu, Yue; Ibrahim, Ashraf S.; Sheppard, Donald C.; Chen, Yee-Chun; French, Samuel W.; Cutler, Jim E.; Filler, Scott G.; Edwards, John E., Jr.
CORPORATE SOURCE: Division of Infectious Diseases, St John's Cardiovascular Research Center, Harbor-UCLA Research and Education Institute, Torrance, CA, 90502, USA
SOURCE: Molecular Microbiology (2002), 44(1), 61-72
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Filamentation and adherence to host cells are crit. virulence factors of **Candida albicans**. Multiple filamentation regulatory pathways have been discovered in C. **albicans** using Saccharomyces cerevisiae as a model. In S. cerevisiae, these pathways converge on Flo11p, which functions as a downstream effector of filamentation and also mediates cell-cell adherence (flocculation). In C. **albicans**, such effector(s) have not yet been identified. Here, we demonstrate that the cell surface protein **Als1p** is an effector of filamentation in C. **albicans**. We show that **Als1p** expression is controlled by the transcription factor Efg1p, which is known to be a key regulator of filamentation in C. **albicans** . Further, disruption of **ALS1** inhibited filamentation, and autonomous expression of **Als1p** restored filamentation in an efg1 homozygous null mutant. Thus, **Als1p** functions as a downstream effector of the EFG1 filamentation pathway. In addn., we found that **Als1p** mediates both flocculation and adherence of C. **albicans** to endothelial cells in vitro. As a cell surface glycoprotein that mediates filamentation and adherence, **Als1p** has both structural and functional similarity to S. cerevisiae Flo11p. Consistent with our in vitro results, **Als1p** was required for both normal filamentation and virulence in the mouse model of hematogenously disseminated candidiasis.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:893299 HCAPLUS
DOCUMENT NUMBER: 136:196745
TITLE: Transcript profiling in **Candida albicans** reveals new cellular functions for the transcriptional repressors CaTup1, CaMig1 and CaNrg1
AUTHOR(S): Murad, A. Munir A.; D'Enfert, Christophe; Gaillardin, Claude; Tournu, Helene; Tekaia, Fredj; Talibi, Driss; Marechal, Daniel; Marchais, Veronique; Cottin, Jane; Brown, Alistair J. P.
CORPORATE SOURCE: Molecular and Cell Biology, Institute of Medical Sciences, University of Aberdeen, Aberdeen, AB25 2ZD, UK
SOURCE: Molecular Microbiology (2001), 42(4), 981-993
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pathogenic fungus, **Candida albicans** contains homologues of the transcriptional repressors ScTup1, ScMig1 and ScNrg1 found in budding yeast. In Saccharomyces cerevisiae, ScMig1 targets the ScTup1/ScSsn6 complex to the promoters of glucose repressed genes to repress their transcription. ScNrg1 is thought to act in a similar manner at other promoters. We have examd. the roles of their homologues in C. **albicans** by transcript profiling with an array contg. 2002 genes, representing about one quarter of the predicted no. of open reading frames (ORFs) in C. **albicans**. The data revealed that CaNrg1 and CaTup1 regulate a different set of C. **albicans** genes from CaMig1 and CaTup1. This is consistent with the idea that CaMig1 and CaNrg1 target the CaTup1 repressor to specific subsets of C. **albicans** genes. However, CaMig1 and CaNrg1 repress other C. **albicans** genes in a CaTup1-independent fashion. The targets of CaMig1 and CaNrg1 repression, and phenotypic analyses of nrg1/nrg1 and mig1/mig1 mutants, indicate that these factors play differential roles in the regulation of metab., cellular morphogenesis and stress responses. Hence, the data provide important information both about the modes of action of these transcriptional regulators and their cellular roles.
REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:658968 HCAPLUS
DOCUMENT NUMBER: 135:341382
TITLE: Biofilm formation by the fungal pathogen **Candida albicans**: development, architecture, and drug resistance
AUTHOR(S): Chandra, Jyotsna; Kuhn, Duncan M.; Mukherjee, Pranab K.; Hoyer, Lois L.; McCormick, Thomas; Ghannoum, Mahmoud A.

CORPORATE SOURCE: Center for Medical Mycology, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, OH, 44106, USA
SOURCE: Journal of Bacteriology (2001), 183(18), 5385-5394
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Biofilms are a protected niche for microorganisms, where they are safe from antibiotic treatment and can create a source of persistent infection. Using 2 clin. relevant C. **albicans** biofilm models formed on bioprosthetic materials, it was demonstrated that biofilm formation proceeds through 3 distinct developmental phases. These growth phases transform adherent blastospores to well-defined cellular communities encased in a polysaccharide matrix. Fluorescence and confocal scanning laser microscopy revealed that C. **albicans** biofilms have a highly heterogeneous architecture composed of cellular and noncellular elements. In both models, antifungal resistance of biofilm-grown cells increased in conjunction with biofilm formation. The expression of **agglutinin-like** (**ALS**) genes, which encode a family of proteins implicated in adhesion to host surfaces, was differentially regulated between planktonic and biofilm-grown cells. The ability of C. **albicans** to form biofilms contrasts sharply with that of Saccharomyces cerevisiae, which adhered to bioprosthetic surfaces but failed to form a mature biofilm. The studies described here form the basis for investigations into the mol. mechanisms of **Candida** biofilm biol. and antifungal resistance and provide the means to design novel therapies for biofilm-based infections.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:353558 HCAPLUS
DOCUMENT NUMBER: 136:96938
TITLE: Characterization of **agglutinin-like** sequence genes from non-**albicans Candida** and phylogenetic analysis of the **ALS** family
AUTHOR(S): Hoyer, Lois L.; Fundyga, Ruth; Hecht, Jennifer E.; Kapteyn, Johan C.; Klis, Frans M.; Arnold, Jonathan
CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Illinois, Urbana, IL, 61802, USA
SOURCE: Genetics (2001), 157(4), 1555-1567
CODEN: GENTAE; ISSN: 0016-6731
PUBLISHER: Genetics Society of America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **ALS** (**agglutinin-like** sequence) gene family of **Candida albicans** encodes cell-surface glycoproteins implicated in adhesion of the organism to host surfaces. As Southern blot anal. with ALS-specific probes suggested the presence of ALS gene families in C. dubliniensis and

C. **tropicalis**; three partial ALS genes were isolated and sequenced from each organism. Northern blot anal. demonstrated that mechanisms governing expression of ALS genes in C. **albicans** and C. dubliniensis are different. Western blots with an anti-Als serum showed that cross-reactive proteins are linked by .beta.1,6-glucan in the cell wall of each non-**albicans** **Candida**, suggesting similar cell wall architecture and conserved processing of Als proteins in these organisms. Although an ALS family is present in each organism, phylogenetic anal. of the C. **albicans**, C. dubliniensis, and C. **tropicalis** ALS genes indicated that, within each species, sequence diversification is extensive and unique ALS sequences have arisen. Phylogenetic anal. of the ALS and SAP (secreted aspartyl proteinase) families show that the ALS family is younger than the SAP family. ALS genes in C. **albicans**, C. dubliniensis, and C. **tropicalis** tend to be located on chromosomes that also encode genes from the SAP family, yet the two families have unexpectedly different evolutionary histories. Homologous recombination between the tandem repeat sequences present in ALS genes could explain the different histories for co-localized genes in a predominantly clonal organism like C. **albicans**.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:77710 HCAPLUS
DOCUMENT NUMBER: 134:322199
TITLE: The ALS5 gene of **Candida** **albicans** and analysis of the Als5p N-terminal domain
AUTHOR(S): Hoyer, L. L.; Hecht, J. E.
CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Illinois, Urbana, IL, 61802, USA
SOURCE: Yeast (2001), 18(1), 49-60
CODEN: YESTE3; ISSN: 0749-503X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB ALS genes of **Candida albicans** encode a family of cell-surface glycoproteins with a three domain structure. Each Als protein has a relatively conserved N-terminal domain, a central domain consisting of a tandemly repeated motif, and a serine-threonine-rich C-terminal domain that is relatively variable across the family. The ALS family exhibits several types of variability that indicate the importance of considering strain and allelic differences when studying ALS genes and their encoded proteins. Anal. of ALS5 provided addnl. evidence of variability within the ALS family. Comparison of the ALS5 sequence from two strains indicated sequence differences larger than strain or allelic mismatches obsd. for other C. **albicans** genes. Screening a collection of commonly used C. **albicans** strains and clin. isolates indicated that ALS5 is not present in several of these strains, supporting the conclusion that the Als protein profile is variable among C. **albicans** isolates. Phys. mapping of ALS5 showed that it is located close to **ALS1** on chromosome 6. The N-terminal domain of Als5p was produced in Pichia pastoris to initiate structural anal. of this portion of the protein. The

hydrophobic character of this portion of the protein was exploited in the purifn. scheme. CD anal. of the purified, authenticated protein yielded a high content of antiparallel .beta.-sheet and little to no .alpha.-helical structure. These results are consistent with the conclusion that the N-terminal domain of Als5p has an Ig fold structure similar to that found in many cell adhesion mols. Gene sequences of C. **albicans** ALS5 (Accession No. AF068866) and TPI1 (Accession No. AF124845) have been deposited in the GenBank database.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:3718 HCAPLUS
DOCUMENT NUMBER: 135:222067
TITLE: Cloning and functional analysis of ALS family genes from **Candida albicans**
AUTHOR(S): Chen, Xi; Chen, Jiang-Ye
CORPORATE SOURCE: State Key Laboratory of Molecular Biology, Shanghai Institute of Biochemistry, the Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China
SOURCE: Shengwu Huaxue Yu Shengwu Wuli Xuebao (2000), 32(6), 586-594
CODEN: SHWPAU; ISSN: 0582-9879
PUBLISHER: Shanghai Kexue Jishu Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB With a 0.5 kb probe of gene CX2 (encoding cytochrome P 450 L1A1 (Lanosterol 14.alpha.-demethylase)), distribution of CX2 tandem repeats was studied in different C. **albicans** strains. Results suggest that all the C. **albicans** strains tested contained the tandem repeat. In order to verify if the expression of CX2 was hyphal specific, its expression was analyzed under various inductive and non-inductive conditions. With CX2 0.5 kb probe, Northern hybridization anal. confirmed that it was specifically in hyphae. The result of chromosomal localization and genomic Southern blot anal. suggested that there were other genes contg. the tandem repeat besides of **ALS1** (**agglutinin-like** sequence). A C. **albicans** 's genomic DNA library was screened with the CX2 0.5 kb probe and several pos. recombinant X phages were obtained. After endonuclease identification, subcloning, and sequence anal., several ALS family genes were cloned. No. 1 X phage DNA contained ALS4, No. 4 X phage DNA contained **ALS1**, No. 6 X phage DNA contained ALS3. To study the role of ALS family genes in yeast-hyphal transition, **als1/ALS1** mutant was constructed by homologous recombination. The ability to form hyphae was tested in different inductive culturing conditions. Defective hyphal growth were obsd. in some solid media.

L2 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:736647 HCAPLUS
DOCUMENT NUMBER: 135:71860
TITLE: Cloning and identification of genes related with morphogenesis of **Candida albicans**

AUTHOR(S): Chen, Xi; Wang, Qin; Chen, Jiang-Ye
CORPORATE SOURCE: State Key Laboratory of Molecular Biology, Shanghai Institute of Biochemistry, The Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China
SOURCE: Shengwu Huaxue Yu Shengwu Wuli Xuebao (2000), 32(5), 509-515
CODEN: SHWPAU; ISSN: 0582-9879
PUBLISHER: Shanghai Kexue Jishu Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A **Candida albicans** cDNA library was constructed and screened by differential hybridization. In hybridization using probes derived from population of yeast cells or hyphae, 67 recombinant phages exhibited more intense signal with the probe derived from hyphae than with the probe from yeast cells. One phage behaved vice versa. Phys. map anal. and nucleotide sequence anal. suggested that cDNA of the CX1, a clone specific for yeast form, is coding for cytochrome P 450 L1A1 (Lanosterol 14.alpha.-demethylase). Its specific expression pattern was confirmed by Northern anal. Inhibition of serum on the expression of CX1 cDNA was obsd. CX2 cDNA was one of those giving intensive signal with hyphae probes. The cDNA sequence contained a tandem repeat sequence, which was also found in **ALS1**, another **Candida albicans** gene identified, whose expression was related with morphogenesis. Northern anal. proved that it was expressed intensively with hyphae probes, however the expression could not be detected in those strongly hybridized to yeast cell probes. The locations of both cDNA on chromosome were analyzed.

L2 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:710707 HCAPLUS
DOCUMENT NUMBER: 133:330262
TITLE: Identification and characterization of genes for protein-mannosyltransferases (CaPMT1, CaPMT6) of the human pathogen fungus **Candida albicans**
AUTHOR(S): Timpel, Claudia
CORPORATE SOURCE: Dusseldorf, Germany
SOURCE: Fortschritt-Berichte VDI, Reihe 17: Biotechnik (1998), 180, i-ix, 1-108
CODEN: FBRBFL; ISSN: 0178-9600
PUBLISHER: VDI Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The protein mannosyltransferase genes CaPMT1 and CAPMT6 were identified in pathogenic **Candida albicans**. Mutants with disruptions in both CaPMT1 alleles showed decreased growth, cell aggregate formation, defective hyphae formation, increased sensitivity towards antimycotics (e.g. hygromycin B, G418, clotrimazol), and decreased adhesion on epithelial cells. They were avirulent in a mouse model of systemic infections. Several cell surface proteins (e.g. chitinase, Als 1 protein) were modified. Heterozygously disrupted C. **albicans** strains and pmt6 mutants were defective in hyphae formation, had an increased sensitivity towards hygromycin B, and a decreased virulence.

REFERENCE COUNT: 196 THERE ARE 196 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE

IN THE RE FORMAT

L2 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:525150 HCAPLUS
DOCUMENT NUMBER: 134:1195
TITLE: The ALS6 and ALS7 genes of **Candida albicans**
AUTHOR(S): Hoyer, L. L.; Hecht, J. E.
CORPORATE SOURCE: Department of Vetennary Pathobiology, University of Illinois, Urbana, IL, 61802, USA
SOURCE: Yeast (2000), 16(9), 847-855
CODEN: YESTE3; ISSN: 0749-503X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ALS genes of **Candida albicans** encode a family of cell-surface glycoproteins that are composed of an N-terminal domain, a central domain of a tandemly repeated motif, and a relatively variable C-terminal domain. Although several ALS genes have been characterized, more ALS-like sequences are present in the C. **albicans** genome. Two short DNA sequences with similarity to the 5' domains of known ALS genes were detected among data from the C. **albicans** genome sequencing project. Probes developed from unique regions of these sequences were used to screen a genomic library from which two full-length genes, designated ALS6 and ALS7, were cloned. ALS6 and ALS7 encode features similar to other genes in the ALS family and map to chromosome 3, a chromosome previously not known to encode ALS sequences. ALS6 and ALS7 are present in all C. **albicans** strains examd. Addnl. anal. suggested that some C. **albicans** strains have another ALS gene with a 5' domain similar to that of ALS6. Characterization of ALS7 revealed a novel tandemly repeated sequence within the C-terminal domain. Unlike other ALS family tandem repeats, the newly characterized ALS7 repeat does not appear to define addnl. genes in the ALS family. However, these data and information from the C. **albicans** genome sequencing project suggest that there are addnl. ALS genes remaining to be characterized. Gene sequences of ALS6 (Accession No. AF075293) and ALS7 (Accession Nos. AF075294 and AF201684) were deposited in the GenBank database.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:376242 HCAPLUS
DOCUMENT NUMBER: 134:144364
TITLE: TUP1, CPH1 and EFG1 make independent contributions to filamentation in **Candida albicans**
AUTHOR(S): Braun, Burkhard R.; Johnson, Alexander D.
CORPORATE SOURCE: Department of Microbiology, University of California, San Francisco, CA, 94143-0414, USA
SOURCE: Genetics (2000), 155(1), 57-67
CODEN: GENTAE; ISSN: 0016-6731
PUBLISHER: Genetics Society of America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The common fungal pathogen, **Candida albicans**, can grow either as single cells or as filaments (hyphae), depending on environmental conditions. Several transcriptional regulators have been identified as having key roles in controlling filamentous growth, including the products of the TUP1, CPH1, and EFG1 genes. We show, through a set of single, double, and triple mutants, that these genes act in an additive fashion to control filamentous growth, suggesting that each gene represents a sep. pathway of control. We also show that environmentally induced filamentous growth can occur even in the absence of all three of these genes, providing evidence for a fourth regulatory pathway. Expression of a collection of structural genes assocd. with filamentous growth, including HYR1, ECE1, HWP1, **ALS1**, and CHS2, was monitored in strains lacking each combination of TUP1, EFG1, and CPH1. Different patterns of expression were obsd. among these target genes, supporting the hypothesis that these three regulatory proteins engage in a network of individual connections to downstream genes and arguing against a model whereby the target genes are regulated through a central filamentous growth pathway. The results suggest the existence of several distinct types of filamentous forms of C. **albicans**, each dependent on a particular set of environmental conditions and each expressing a unique set of surface proteins.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:129195 HCAPLUS
DOCUMENT NUMBER: 132:248349
TITLE: The cell wall architecture of **Candida albicans** wild-type cells and cell wall-defective mutants
AUTHOR(S): Kapteyn, J. C.; Hoyer, L. L.; Hecht, J. E.; Muller, W. H.; Andel, A.; Verkleij, A. J.; Makarow, M.; Van Den Ende, H.; Klis, F. M.
CORPORATE SOURCE: Swammerdam Institute of Life Sciences, University of Amsterdam, Amsterdam, 1098 SM, Neth.
SOURCE: Molecular Microbiology (2000), 35(3), 601-611
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In **Candida albicans** wild-type cells, the .beta.1,6-glucanase-extractable glycosylphosphatidylinositol (GPI)-dependent cell wall proteins (CWPs) account for about 88% of all covalently linked CWPs. Approx. 90% of these GPI-CWPs, including **Als1p** and Als3p, are attached via .beta.1,6-glucan to .beta.1,3-glucan. The remaining GPI-CWPs are linked through .beta.1,6-glucan to chitin. The .beta.1,6-glucanase-resistant protein fraction is small and consists of Pir-related CWPs, which are attached to .beta.1,3-glucan through an alkalilabile linkage. Immunogold labeling and Western anal., using an antiserum directed against Saccharomyces cerevisiae Pir2p/Hsp150, point to the localization of at least two differentially expressed Pir2 homologues in the cell wall of C. **albicans**. In mnn9.DELTA. and pmt1.DELTA. mutant strains, which are defective in

N- and O-glycosylation of proteins resp., we obsd. enhanced chitin levels together with an increased coupling of GPI-CWPs through .beta.1,6-glucan to chitin. In these cells, the level of Pir-CWPs was slightly upregulated. A slightly increased incorporation of Pir proteins was also obsd. in a .beta.1,6-glucan-deficient hemizygous kre6.DELTA. mutant. Taken together, these observations show that C. **albicans** follows the same basic rules as S. cerevisiae in constructing a cell wall and indicate that a cell wall salvage mechanism is activated when **Candida** cells are confronted with cell wall weakening.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:578611 HCAPLUS
DOCUMENT NUMBER: 131:283671
TITLE: Adhesins in **Candida albicans**
AUTHOR(S): Sundstrom, Paula
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, Ohio State University Columbus, Columbus, OH, 43210-1239, USA
SOURCE: Current Opinion in Microbiology (1999), 2(4), 353-357
CODEN: COMIF7; ISSN: 1369-5274
PUBLISHER: Current Biology Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 35 refs. The adherent properties of **Candida albicans** blasloconidia and germ tubes have long been appreciated, but little is known about the mechanisms responsible for adherence. Recently, three genes, ALA1, **ALS1** and HWP1, encoding proteins with adherent properties and motifs consistent with linkage to the .beta.-1,6-glucan of C. **albicans** cell walls have provided insight into the topol. of protein adhesins. Hwp1, a developmentally regulated adhesin of germ tubes and hyphae, attaches to buccal epithelial cells by an unconventional, transglutaminase-mediated mechanism of adhesion.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:729949 HCAPLUS
DOCUMENT NUMBER: 130:137543
TITLE: Up-regulation of two **Candida albicans** genes in the rat model of oral candidiasis detected by differential display
AUTHOR(S): Zhao, Xiao-Jiong; Newsome, Joseph T.; Cihlar, Ronald L.
CORPORATE SOURCE: Department of Microbiology and Immunology, Georgetown University, Washington, DC, 20007, USA
SOURCE: Microbial Pathogenesis (1998), 25(3), 121-129
CODEN: MIPAEV; ISSN: 0882-4010
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Candida albicans** is an opportunistic fungal pathogen responsible for the largest percentage of fungal-mediated oral and esophageal disease. In this regard, knowledge concerning patterns of gene expression during the establishment and/or maintenance of infection may be the key to the design of new strategies for treatment, as well as providing insight into pathogenesis. To address this issue, expts. were performed that utilized differential display to compare the spectrum of C. **albicans** genes expressed during oral infection vs. growth in in vitro culture. Exptl., the rat model of oral candidiasis served as the in vivo source. After initiation of infection and subsequent harvesting of C. **albicans** from the rat oral cavity, RNA was isolated, and used with a small no. of primers in reverse-transcriptase polymerase chain reaction (RT-PCR) and differential display expts. Fragments unique to in vivo samples were subcloned and sequenced. Southern blot anal. verified the origin of seven fragments as from C. **albicans**. Addnl., specific RT-PCR confirmed that two of these fragments represented genes that were up-regulated during C. **albicans** in vivo growth in the rat model. Database searches indicated the fragments share homol. with a member of the C. **albicans** agglutinin gene family and to a bacterial gene (gidB) possibly involved in cell division. (c) 1998 Academic Press.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:681160 HCAPLUS

DOCUMENT NUMBER: 130:22640

TITLE: Identification of **Candida albicans** ALS2 and ALS4 and localization of Als proteins to the fungal cell surface

AUTHOR(S): Hoyer, L. L.; Payne, T. L.; Hecht, J. E.

CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Illinois, Urbana, IL, 61802, USA

SOURCE: Journal of Bacteriology (1998), 180(20), 5334-5343
CODEN: JOBAAY; ISSN: 0021-9193

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Addnl. genes in the growing **ALS** (**agglutinin-like** sequence) family of **Candida albicans** were isolated by PCR screening of a genomic fosmid library with primers designed from the consensus tandem-repeat sequence of **ALS1**. This procedure yielded fosmids encoding ALS2 and ALS4. ALS2 and ALS4 conformed to the three-domain structure of ALS genes, which consists of a central domain of tandemly repeated copies of a 108-bp motif, an upstream domain of highly conserved sequences, and a domain of divergent sequences 3' of the tandem repeats. Alignment of five predicted Als protein sequences indicated conservation of N- and C-terminal hydrophobic regions which have the hallmarks of secretory signal sequences and glycosylphosphatidylinositol addn. sites, resp. Heterologous expression of an N-terminal fragment of **Als1p** in Saccharomyces cerevisiae demonstrated function of the putative signal sequence with cleavage following Ala17. This signal sequence

cleavage site was conserved in the four other Als proteins analyzed, suggesting identical processing of each protein. Primary-structure features of the five Als proteins suggested a cell-surface localization, which was confirmed by indirect immunofluorescence with an anti-Als antiserum. Staining was obsd. on mother yeasts and germ tubes, although the intensity of staining on the mother yeast decreased with elongation of the germ tube. Similar to other ALS genes, ALS2 and ALS4 were differentially regulated. ALS4 expression was correlated with the growth phase of the culture; ALS2 expression was not obsd. under many different in vitro growth conditions. The data presented here demonstrate that ALS genes encode cell-surface proteins and support the conclusion that the size and no. of Als proteins on the C. **albicans** cell surface vary with strain and growth conditions.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:557795 HCAPLUS
DOCUMENT NUMBER: 129:257448
TITLE: Multiple functions of Pmt1p-mediated protein O-mannosylation in the fungal pathogen **Candida albicans**
AUTHOR(S): Timpel, Claudia; Strahl-Bolsingers, Sabine; Ziegelbauer, Karl; Ernst, Joachim F.
CORPORATE SOURCE: Institut fur Mikrobiologie und Biologisch-Medizinisches Forschungszentrum, Heinrich-Heine-Universitat, Dusseldorf, D-40225, Germany
SOURCE: Journal of Biological Chemistry (1998), 273(33), 20837-20846
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Protein mannosylation by Pmt proteins initiates O-glycosylation in fungi. We have identified the PMT1 gene and analyzed the function of Pmt1p in the fungal human pathogen **Candida albicans**. Mutants defective in PMT1 alleles lacked Pmt in vitro enzymic activity, showed reduced growth rates, and tended to form cellular aggregates. In addn., multiple specific deficiencies not known in Saccharomyces cerevisiae (including defective hyphal morphogenesis; supersensitivity to the antifungal agents hygromycin B, G418, clotrimazole, and calcofluor white; and reduced adherence to Caco-2 epithelial cells) were obsd. in pmt1 mutants. PMT1 deficiency also led to faster electrophoretic mobility of the **Als1p** cell wall protein and to elevated extracellular activities of chitinase. Homozygous pmt1 mutants were avirulent in a mouse model of systemic infection, while heterozygous PMT1/pmt1 strains showed reduced virulence. The results indicate that protein O-mannosylation by Pmt proteins occurs in different fungal species, where PMT1 deficiency can lead to defects in multiple cellular functions.

L2 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:399926 HCAPLUS

DOCUMENT NUMBER: 129:326716
TITLE: **Candida albicans** ALS3 and insights into the nature of the ALS gene family
AUTHOR(S): Hoyer, L. L.; Payne, Tracie L.; Bell, M.; Myers, Alan M.; Scherer, S.
CORPORATE SOURCE: 2522 VMBSB, Department of Veterinary Pathobiology, University of Illinois at Urbana-Champaign, 2001 S. Lincoln Avenue, Urbana, IL, 61802, USA
SOURCE: Current Genetics (1998), 33(6), 451-459
CODEN: CUGED5; ISSN: 0172-8083
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **ALS1** (**agglutinin-like** sequence) gene of **Candida albicans** encodes a protein similar to alpha-agglutinin, a cell-surface adhesion glycoprotein of Saccharomyces cerevisiae (Hoyer et al. 1995). A central domain of a tandemly repeated 108-bp sequence is found in the **ALS1** coding region. This tandem-repeat motif hybridizes to multiple C. **albicans** genomic DNA fragments, indicating the possibility of other **ALS1**-like genes in C. **albicans** (Hoyer et al. 1995). To det. if these fragments constitute a gene family, tandem-repeat-hybridizing genomic fragments were isolated from a fosmid library by PCR screening using primers based on the consensus tandem-repeat sequence of **ALS1** (Hoyer et al. 1995). One group of fosmids, designated ALS3, encodes a gene with 81% identity to **ALS1**. The sequences of **ALS1** and ALS3 are most conserved in the tandem-repeat domain and in the region 5' of the tandem repeats. Northern-blot anal. using unique probes from the 3' end of each gene demonstrated that **ALS1** expression varies, depending on which C. **albicans** strain is examd., and that ALS3 is hyphal-specific. Both genes are found in a variety of C. **albicans** and C. stellatoidea strains examd. The predicted **Als1p** and Als3p exhibit features suggesting that both are cell-surface glycoproteins. Southern blots probed with conserved sequences from the region 5' of the tandem repeats suggest that other ALS-like sequences are present in the C. **albicans** genome and that the ALS family may be larger than originally estd.

L2 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:214170 HCAPLUS
DOCUMENT NUMBER: 128:320030
TITLE: Expression of the **Candida albicans** gene **ALS1** in Saccharomyces cerevisiae induces adherence to endothelial and epithelial cells
AUTHOR(S): Fu, Yue; Rieg, Gunter; Fonzi, William A.; Belanger, Paul H.; Edwards, John E., Jr.; Filler, Scott G.
CORPORATE SOURCE: St. John's Cardiovascular Research Center, Division of Infectious Diseases, Department of Medicine, Harbor-UCLA Research and Education Institute, Torrance, CA, 90502, USA
SOURCE: Infection and Immunity (1998), 66(4), 1783-1786
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal

LANGUAGE: English

AB To identify genes encoding adhesins that mediate the binding of **Candida albicans** to endothelial cells, a genomic library from this organism was constructed and used to transform Saccharomyces cerevisiae. These transformed organisms were screened for adherence to endothelial cells, and a highly adherent clone was identified. The adherence of this clone to endothelial cells was over 100-fold greater than that of control S. cerevisiae transformed with the empty plasmid. This clone also exhibited enhanced adherence to epithelial cells. The C. **albicans** gene contained within this clone was **ALS1**. These results indicate that **ALS1** may encode a candidal adhesin.

L2 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:773548 HCAPLUS

DOCUMENT NUMBER: 128:98314

TITLE: Expression, cloning, and characterization of a **Candida albicans** gene, ALA1, that confers adherence properties upon Saccharomyces cerevisiae for extracellular matrix proteins

AUTHOR(S): Gaur, Nand K.; Klotz, Stephen A.

CORPORATE SOURCE: Research Service, Veterans Affairs Medical Center, Kansas City, MO, USA

SOURCE: Infection and Immunity (1997), 65(12), 5289-5294
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Adherence of **Candida albicans** to host tissues is a necessary step for maintenance of its commensal status and is likely a necessary step in the pathogenesis of candidiasis. The extracellular matrix (ECM) proteins are some of the host tissue and plasma proteins to which C. **albicans** adheres through adhesins located on the fungal cell surface. To isolate genes encoding ECM adhesins, an assay was developed based on the ability of yeast cells to adhere to magnetic beads coated with the ECM protein fibronectin, type IV collagen, or laminin. A C. **albicans** genomic library was constructed by cloning XbaI-partially-digested and size-selected fragments into pAUR112, an Escherichia coli-yeast low-copy-no. shuttle vector. The C. **albicans** library was transformed into Saccharomyces cerevisiae YPH 499, and clones capable of adherence were selected by using ECM protein-coated magnetic beads. A plasmid contg. an .apprx.-8-kb insert was isolated from 29 adherent clones. These clones exhibited adherence to all ECM protein-coated magnetic beads and to human buccal epithelial cells. The ALAI gene (for **agglutinin-like** adhesin) was localized by subcloning it into a 5-kb XbaI fragment which retained the adherence phenotype in both orientations. The complete DNA sequence of the 5-kb insert was detd., and an open reading frame (ORF) encoding 1,419 amino acid residues was identified. Deletions from the 5' and 3' ends extending into the DNA sequence encoding the 1,419-amino-acid ORF product inactivated the adherence phenotype, suggesting that it is the coding region of the ALA1 gene. A database search identified ALA1 to be similar to the C. **albicans ALS1** (for **agglutinin-like** sequence 1) protein and the S. cerevisiae agglutinin

protein (AG.alpha.1), although the homol. at the primary amino acid sequence level is limited to the first half of each of these proteins. ALA1 contains a central domain of six tandem repeats of 36 amino acids. We discuss the significance of various predicted ALA1 structural motifs and their relation- ships to function in the adherence process.

L2 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:473241 HCAPLUS
DOCUMENT NUMBER: 125:134790
TITLE: **Candida albicans** and C. stellatoidea gene **ALS1** PCR primers and probes for infection diagnosis
INVENTOR(S): Hoyer, Lois L.; Livi, George P.; Shatzman, Allan
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9618745	A1	19960620	WO 1995-US16153	19951208
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, PT, RO, RU, SD, SG, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5668263	A	19970916	US 1994-357962	19941216
CA 2207816	AA	19960620	CA 1995-2207816	19951208
AU 9644686	A1	19960703	AU 1996-44686	19951208
EP 820523	A1	19980128	EP 1995-943412	19951208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
ZA 9501645	A	19960904	ZA 1995-10645	19951214
US 5817466	A	19981006	US 1997-878106	19970618

PRIORITY APPLN. INFO.: US 1994-357962 19941216
WO 1995-US16153 19951208

AB This invention relates to nucleic acid sequences conserved in strains of yeasts. More particularly, this invention relates to segments of the **ALS1** gene of **Candida albicans** useful as probes and primers for the identification of yeast, particularly **Candida**, infections.

L2 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:301691 HCAPLUS
DOCUMENT NUMBER: 122:179968
TITLE: **Candida albicans** **ALS1**: domains related to a Saccharomyces cerevisiae sexual agglutinin separated by a repeating motif
AUTHOR(S): Hoyer, L. L.; Scherer, S.; Shatzman, A. R.; Livi, G. P.
CORPORATE SOURCE: Human Genome Cent., Lawrence Berkeley Lab., Berkeley, CA, 94720, USA
SOURCE: Molecular Microbiology (1995), 15(1), 39-54

CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Transfer of budding **Candida albicans** yeast cells from the rich, complex medium YEPD to the defined tissue culture medium RPMI 1640 (RPMI) at 37.degree. and 5% CO2 causes rapid onset of hyphal induction. Among the genes induced under these conditions are hyphal-specific genes as well as genes expressed in response to changes in temp., CO2, and specific media components. A cDNA library constructed from cells incubated for 20 min in RPMI was differentially screened with yeast (YEPD)- and hyphal (RPMI)-specific probes resulting in identification of a gene expressed in response to culture conditions but not regulated by the yeast-hyphal transition. The deduced gene product displays significant identity to Saccharomyces cerevisiae .alpha.-agglutinin, encoded by AG.alpha.1, an adhesion glycoprotein that mediates mating of haploid cells. The presence of this gene in C. **albicans** is curious since the organism has not been obsd. to undergo meiosis. The C. **albicans** gene was designated **ALS1** (for **agglutinin-like** sequence). Although the N- and C-termini of the predicted 1260-amino-acid **ALS1** protein resemble those of the 650-amino-acid AG.alpha.1, **ALS1** contains a central domain of tandem repeats consisting of a highly conserved 36-amino-acid sequence not present in AG.alpha.1. These repeats are also present on the nucleotide level as a highly conserved 108-bp motif. Southern and Northern blot analyses indicate a family of C. **albicans** genes that contain the tandem repeat motif; at least one gene in addn. to **ALS1** is expressed under conditions similar to those for **ALS1** expression. Genomic Southern blots from several C. **albicans** isolates indicate that the no. of copies of the tandem repeat element in **ALS1** differs across strains and, in some cases, between **ALS1** alleles in the same strain, suggesting a strain-dependent variability in **ALS1** protein size. Potential roles for the **ALS1** protein are discussed.

L2 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1979:414474 HCAPLUS
DOCUMENT NUMBER: 91:14474
TITLE: Antibiotics and antiseptic compounds from the family Bonnemaisoniaceae (Florideophyceae)
AUTHOR(S): Fenical, William; McConnell, Oliver J.; Stone, Anne
CORPORATE SOURCE: Inst. Mar. Resour., Scripps Inst. Oceanogr., La Jolla, CA, 92093, USA
SOURCE: Proc. Int. Seaweed Symp. (1979), Volume Date 1977, 9, 387-400
CODEN: ISSYA4; ISSN: 0074-7874
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Components of Bonnemaisonia asparagoides, B. nootkana, Asparagopsis taxiformis, and A. armata have antibacterial and antifungal activity. These components are active against both Staphylococcus aureus and **Candida alsicans**, with only slight activity against Escherichia coli and Vibrio anguillarium. The halobutenones and Et dibromoacrylate [63881-48-1] from Asparagopsis showed significantly greater activity against C. **albicans**

than S. aureus. Almost all of the compds. were at least slightly active against .gtoreq.1 pathogens.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, TOXCENTER, PHIC, PHIN' ENTERED AT 09:53:19 ON 07 OCT 2002)
L3 58 S L2
L4 27 DUP REM L3 (31 DUPLICATES REMOVED)

L4 ANSWER 1 OF 27 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002426471 MEDLINE
DOCUMENT NUMBER: 22170774 PubMed ID: 12183577
TITLE: Contribution of **Candida albicans ALS1** to the pathogenesis of experimental oropharyngeal candidiasis.
AUTHOR: Kamai Yasuki; Kubota Mikie; Kamai Yoko; Hosokawa Tsunemichi; Fukuoka Takashi; Filler Scott G
CORPORATE SOURCE: Biological Research Laboratory, Sankyo Co., Ltd., Shinagawa-ku, Tokyo 140-8710, Japan.. ykamai@shina.sankyo.co.jp
CONTRACT NUMBER: P01 AI37194 (NIAID)
R01 AI19990 (NIAID)
R01 DE13974 (NIDCR)
SOURCE: INFECTION AND IMMUNITY, (2002 Sep) 70 (9) 5256-8. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020817
Last Updated on STN: 20020919
Entered Medline: 20020918
AB We investigated the contribution of **Candida albicans ALS1**, which encodes a candidal adhesin, to the pathogenesis of experimental murine oropharyngeal candidiasis. Our results indicate that the **ALS1** gene product is important for the adherence of the organism to the oral mucosa during the early stage of the infection.

L4 ANSWER 2 OF 27 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002307159 EMBASE
TITLE: Evaluation of the antimicrobial potential of medicinal plants from the ivory coast.
AUTHOR: Kamanzi Atindehou K.; Kone M.; Terreaux C.; Traore D.; Hostettmann K.; Dosso M.
CORPORATE SOURCE: K. Hostettmann, Inst. of Pharmacognosy/Phytochem., BEP, University of Lausanne, CH-1015 Lausanne, Switzerland. kurt.hostettmann@ipp.unil.ch
SOURCE: Phytotherapy Research, (2002) 16/5 (497-502). Refs: 19
ISSN: 0951-418X CODEN: PHYREH
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A total of 148 crude ethanol extracts from 115 plant species were tested in vitro against Gram-negative strains (Escherichia coli, Pseudomonas aeruginosa) and the Gram-positive Staphylococcus aureus and Enterococcus faecalis. Moreover, they were submitted to antifungal assays against **Candida albicans** and Cladosporium cucumerinum, a human and a plant pathogenic microorganism, respectively, known to be good indicators of antifungal activity. No activity was detected against the Gram-negative bacteria, while 14.8% and 10.8% of the extracts showed Gram-positive bactericidal or bacteriostatic effects on S. aureus and E. faecalis, respectively. An antifungal activity was observed with 15 extracts (10.1%). Two species were particularly active against the fungi: Dioscorea minutiflora and Erythrina vogelii. The young tubers of D. minutiflora contain metabolites with a specific effect on fungi and were not active against the bacteria. On the other hand, E. vogelii was highly effective against the Gram-positive bacteria and the fungi. Copyright .COPYRGT. 2002 John Wiley & Sons, Ltd.

L4 ANSWER 3 OF 27 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002419655 IN-PROCESS
DOCUMENT NUMBER: 22164023 PubMed ID: 12174081
TITLE: Adhesion in **Candida** spp.
AUTHOR: Sundstrom Paula
CORPORATE SOURCE: Department of Molecular Virology, Immunology and Medical Genetics, and the Department of Microbiology, The Ohio State University College of Medicine, Columbus, OH 43210-1239, USA.
SOURCE: CELLULAR MICROBIOLOGY, (2002 Aug) 4 (8) 461-9. Journal code: 100883691. ISSN: 1462-5814.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020814
Last Updated on STN: 20020814

AB Microbial adherence is one of the most important determinants of pathogenesis, yet very few adhesins have been identified from fungal pathogens. Four structurally related adhesins, Hwp1, Ala1p/Als5p, **Als1p**, from **Candida albicans** and Epa1p from **Candida** glabrata, are members of a class of proteins termed glycosylphosphatidylinositol-dependent cell wall proteins (GPI-CWP). These proteins have N-terminal signal peptides and C-terminal features that mediate glycosylphosphatidylinositol (GPI) membrane anchor addition, as well as other determinants leading to attachment to cell wall glucan. While common signalP/GPI motifs facilitate cell surface expression, unique features mediate ligand binding specificities of adhesins. The first glimpse of structural features of putative adhesins has come from biophysical characterizations of the N-terminal domain of Als5p. One protein not in the GPI-CWP class that was initially described as an adhesin, Int1p, has recently been shown to be similar to Bud4p of Saccharomyces cerevisiae in primary amino acid sequence, in co-localizing with septins and in functioning in bud site selection. Progress in understanding the role of adhesins in oroesophageal candidiasis has been made for Hwp1 in a study using beige athymic and transgenic varepsilon 26 mice that have combined defects in innate and acquired immune responses. Searches of the C.

albicans genome for proteins in the GPI-CWP class has led to the identification of a subset of genes that will be the focus of future efforts to identify new **Candida** adhesins.

L4 ANSWER 4 OF 27 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002317805 EMBASE
TITLE: Evaluation of Evolvulus **alsinoides** Linn. for anthelmintic and antimicrobial activities.
AUTHOR: Dash G.K.; Suresh P.; Sahu S.K.; Kar D.M.; Ganapaty S.; Panda S.B.
CORPORATE SOURCE: G.K. Dash, Institute of Pharmacy and Technology, Salipur, Cuttack District, Orissa-754202, India. gk_dash@rediffmail.com
SOURCE: Journal of Natural Remedies, (2002) 2/2 (182-185). Refs: 10
ISSN: 0972-5547 CODEN: JNROAD
COUNTRY: India
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective: To study the anthelmintic and antimicrobial activities of the ethanolic extract of Evolvulus **alsinoides** Linn. Materials and methods: The anthelmintic activity was evaluated on adult Indian earthworm Pheretima posthuma due to its anatomical and physiological resemblance with the intestinal roundworm parasites of human beings. The antibacterial activity of the crude ethanolic extract was performed by agar cup plate method. Results: The ethanolic extract caused paralysis followed by death of the worms at all tested dose levels. It was observed that the ethanolic extract of Evolvulus **alsinoides** is more potent than the reference control piperazine citrate. Potency of the extract was inversely proportional to the time taken for paralysis/ death of the worms. The activity confirms the dose dependency nature of the extract. The results of antimicrobial activity revealed that the extract exhibited activity against Pseudomonas aeruginosa and Escherichia coli but inactive against Staphyloccus aureus and **Candida albicans**. None of test concentrations exhibited comparable activity with the reference control ampicillin trihydrate. Conclusion: The present study concludes that the plant is also endowed with potential anthelmintic property in addition to its other popular uses in the traditional system of medicine.

L4 ANSWER 5 OF 27 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2002230107 MEDLINE
DOCUMENT NUMBER: 21964592 PubMed ID: 11967069
TITLE: **Candida albicans Als1p**: an adhesin that is a downstream effector of the EFG1 filamentation pathway.
AUTHOR: Fu Yue; Ibrahim Ashraf S; Sheppard Donald C; Chen Yee-Chun; French Samuel W; Cutler Jim E; Filler Scott G; Edwards John E Jr
CORPORATE SOURCE: Division of Infectious Diseases, St John's Cardiovascular Research Center, Harbor-UCLA Research and Education Institute, Bldg. RB2, 1124 West Carson St., Torrance, CA 90502, USA.. Fue_Yu@humc.edu

CONTRACT NUMBER: 1S10 RR 13004 (NCRR)
M01 RR 00425 (NCRR)
P01 AI 37194 (NIAID)
R01 AI 19990 (NIAID)
R29 AI 40636 (NIAID)
SOURCE: MOLECULAR MICROBIOLOGY, (2002 Apr) 44 (1) 61-72.
Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020423
Last Updated on STN: 20020817
Entered Medline: 20020816

AB Filamentation and adherence to host cells are critical virulence factors of **Candida albicans**. Multiple filamentation regulatory pathways have been discovered in C. **albicans** using Saccharomyces cerevisiae as a model. In S. cerevisiae, these pathways converge on Flo11p, which functions as a downstream effector of filamentation and also mediates cell-cell adherence (flocculation). In C. **albicans**, such effector(s) have not yet been identified. Here, we demonstrate that the cell surface protein **Als1p** is an effector of filamentation in C. **albicans**. We show that **Als1p** expression is controlled by the transcription factor Efg1p, which is known to be a key regulator of filamentation in C. **albicans**. Further, disruption of **ALS1** inhibited filamentation, and autonomous expression of **Als1p** restored filamentation in an efg1 homozygous null mutant. Thus, **Als1p** functions as a downstream effector of the EFG1 filamentation pathway. In addition, we found that **Als1p** mediates both flocculation and adherence of C. **albicans** to endothelial cells in vitro. As a cell surface glycoprotein that mediates filamentation and adherence, **Als1p** has both structural and functional similarity to S. cerevisiae Flo11p. Consistent with our in vitro results, **Als1p** was required for both normal filamentation and virulence in the mouse model of haematogenously disseminated candidiasis.

L4 ANSWER 6 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:486896 BIOSIS
DOCUMENT NUMBER: PREV200200486896
TITLE: Expression analysis of **Agglutinin-Like** Sequence 1 of **Candida albicans**.
AUTHOR(S): Ibrahim, A. S. (1); Sheppard, D. C. (1); Fu, Y. (1); Edwards, J. E., Jr. (1)
CORPORATE SOURCE: (1) Harbor-UCLA Research and Education Institute, Torrance, CA USA
SOURCE: International Journal of Infectious Diseases, (June, 2002) Vol. 6, No. Supplement 2, pp. 2S47. http://www.isid.org/publications/ijid.shtml. print. Meeting Info.: 12th International symposium on infections in the immunocompromised host Bergen, Norway June 23-26, 2002 International Immunocompromised Host Society . ISSN: 1201-9712.

DOCUMENT TYPE: Conference
LANGUAGE: English

L4 ANSWER 7 OF 27 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001469560 MEDLINE
DOCUMENT NUMBER: 21405741 PubMed ID: 11514524
TITLE: Biofilm formation by the fungal pathogen **Candida albicans**: development, architecture, and drug resistance.
AUTHOR: Chandra J; Kuhn D M; Mukherjee P K; Hoyer L L; McCormick T; Ghannoum M A
CORPORATE SOURCE: Center for Medical Mycology, University Hospitals of Cleveland, and Department of Dermatology, Case Western Reserve University, Cleveland, Ohio 44106, USA.
CONTRACT NUMBER: AI-36219 (NIAID)
AI35097-03 (NIAID)
AIO7024 (NIAID)
RO1-DE13992 (NIDCR)
SOURCE: JOURNAL OF BACTERIOLOGY, (2001 Sep) 183 (18) 5385-94. Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010830
Last Updated on STN: 20011001
Entered Medline: 20010927

AB Biofilms are a protected niche for microorganisms, where they are safe from antibiotic treatment and can create a source of persistent infection. Using two clinically relevant **Candida albicans** biofilm models formed on bioprosthetic materials, we demonstrated that biofilm formation proceeds through three distinct developmental phases. These growth phases transform adherent blastospores to well-defined cellular communities encased in a polysaccharide matrix. Fluorescence and confocal scanning laser microscopy revealed that C. **albicans** biofilms have a highly heterogeneous architecture composed of cellular and noncellular elements. In both models, antifungal resistance of biofilm-grown cells increased in conjunction with biofilm formation. The expression of **agglutinin-like** (**ALS**) genes, which encode a family of proteins implicated in adhesion to host surfaces, was differentially regulated between planktonic and biofilm-grown cells. The ability of C. **albicans** to form biofilms contrasts sharply with that of Saccharomyces cerevisiae, which adhered to bioprosthetic surfaces but failed to form a mature biofilm. The studies described here form the basis for investigations into the molecular mechanisms of **Candida** biofilm biology and antifungal resistance and provide the means to design novel therapies for biofilm-based infections.

L4 ANSWER 8 OF 27 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001394889 MEDLINE
DOCUMENT NUMBER: 21186039 PubMed ID: 11290712
TITLE: Characterization of **agglutinin-like** sequence genes from non-**albicans** **Candida** and phylogenetic analysis of the

ALS family.

AUTHOR: Hoyer L L; Fundyga R; Hecht J E; Kapteyn J C; Klis F M; Arnold J
CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Illinois, Urbana, Illinois 61802, USA..
lhoyer@uiuc.edu

CONTRACT NUMBER: AI39441 (NIAID)
T32-AI07373 (NIAID)
SOURCE: GENETICS, (2001 Apr) 157 (4) 1555-67.
Journal code: 0374636. ISSN: 0016-6731.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010716
Last Updated on STN: 20010716
Entered Medline: 20010712

AB The **ALS** (**agglutinin-like** sequence) gene family of **Candida albicans** encodes cell-surface glycoproteins implicated in adhesion of the organism to host surfaces. Southern blot analysis with **ALS**-specific probes suggested the presence of **ALS** gene families in C. dubliniensis and C. **tropicalis**; three partial **ALS** genes were isolated from each organism. Northern blot analysis demonstrated that mechanisms governing expression of **ALS** genes in C. **albicans** and C. dubliniensis are different. Western blots with an anti-**Als** serum showed that cross-reactive proteins are linked by beta 1,6-glucan in the cell wall of each non-**albicans Candida**, suggesting similar cell wall architecture and conserved processing of **Als** proteins in these organisms. Although an **ALS** family is present in each organism, phylogenetic analysis of the C. **albicans**, C. dubliniensis, and C. **tropicalis** **ALS** genes indicated that, within each species, sequence diversification is extensive and unique **ALS** sequences have arisen. Phylogenetic analysis of the **ALS** and SAP (secreted aspartyl proteinase) families show that the **ALS** family is younger than the SAP family. **ALS** genes in C. **albicans**, C. dubliniensis, and C. **tropicalis** tend to be located on chromosomes that also encode genes from the SAP family, yet the two families have unexpectedly different evolutionary histories. Homologous recombination between the tandem repeat sequences present in **ALS** genes could explain the different histories for co-localized genes in a predominantly clonal organism like C. **albicans**.

L4 ANSWER 9 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:402713 BIOSIS
DOCUMENT NUMBER: PREV200100402713
TITLE: The ALS gene family of **Candida albicans**.

AUTHOR(S): Hoyer, Lois L. (1)
CORPORATE SOURCE: (1) Dept of Veterinary Pathobiology, University of Illinois at Urbana-Champaign, 2001 S. Lincoln Avenue, Urbana, IL, 61802: lhoyer@uiuc.edu USA

SOURCE: Trends in Microbiology, (April, 2001) Vol. 9, No. 4, pp. 176-180. print.

ISSN: 0966-842X.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The ALS gene family of **Candida albicans** encodes large cell-surface glycoproteins that are implicated in the process of adhesion to host surfaces. ALS genes are also found in other **Candida** species that are isolated from cases of clinical disease. Genes in the ALS family are differentially regulated by physiologically relevant mechanisms. ALS genes exhibit several levels of variability including strain- and allele-specific size differences for the same gene, strain-specific differences in gene regulation, the absence of particular ALS genes in certain isolates, and additional ALS coding regions in others. The differential regulation and genetic variability of the ALS genes results in a diverse cell-surface Als protein profile that is also affected by growth conditions. The ALS genes are one example of a gene family associated with pathogenicity mechanisms in C. **albicans** and other **Candida** species.

L4 ANSWER 10 OF 27 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001126199 MEDLINE
DOCUMENT NUMBER: 21064501 PubMed ID: 11124701
TITLE: The ALS5 gene of **Candida albicans** and analysis of the Als5p N-terminal domain.
AUTHOR: Hoyer L L; Hecht J E
CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Illinois, Urbana, IL 61802, USA.. lhoyer@uiuc.edu
CONTRACT NUMBER: AI39441 (NIAID)
RR07141 (NCRR)
SOURCE: YEAST, (2001 Jan 15) 18 (1) 49-60.
Journal code: 8607637. ISSN: 0749-503X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF068866; GENBANK-AF124845
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010222
AB ALS genes of **Candida albicans** encode a family of cell-surface glycoproteins with a three-domain structure. Each Als protein has a relatively conserved N-terminal domain, a central domain consisting of a tandemly repeated motif, and a serine-threonine-rich C-terminal domain that is relatively variable across the family. The ALS family exhibits several types of variability that indicate the importance of considering strain and allelic differences when studying ALS genes and their encoded proteins. Analysis of ALS5 provided additional evidence of variability within the ALS family. Comparison of the ALS5 sequence from two strains indicated sequence differences larger than strain or allelic mismatches observed for other C. **albicans** genes. Screening a collection of commonly used C. **albicans** strains and clinical isolates indicated that ALS5 is not present in several of these strains, supporting the conclusion that the Als protein profile is variable among C. **albicans** isolates. Physical mapping of ALS5 showed that it is located close to

ALS1 on chromosome 6. The N-terminal domain of Als5p was produced in Pichia pastoris to initiate structural analysis of this portion of the protein. The hydrophobic character of this portion of the protein was exploited in the purification scheme. Circular dichroism analysis of the purified, authenticated protein yielded a high content of antiparallel beta-sheet and little to no alpha-helical structure. These results are consistent with the conclusion that the N-terminal domain of Als5p has an immunoglobulin fold structure similar to that found in many cell adhesion molecules. Gene sequences of C. **albicans** ALS5 (Accession No. AF068866) and TPI1 (Accession No. AF124845) have been deposited in the GenBank database.

L4 ANSWER 11 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:347251 BIOSIS
DOCUMENT NUMBER: PREV200000347251
TITLE: Gene regulation during morphogenesis in **Candida albicans**.
AUTHOR(S): Brown, Alistair J. P. (1); Barelle, Caroline J.; Budge, Susan; Duncan, James; Harris, Sheila; Lee, Philip R.; Leng, Ping; Macaskill, Susan; Murad, A. M. A.; Ramsdale, Mark; Wiltshire, Carolyn; Sishart, Jill A.; Gow, Neil A. R.
CORPORATE SOURCE: (1) Department of Molecular and Cell Biology, Institute of Medical Sciences, University of Aberdeen, Aberdeen, Foresterhill, AB25 2ZD UK
SOURCE: Ernst, Joachim F.; Schmidt, Axel. Contributions to Microbiology, (2000) Vol. 5, pp. 112-125. Contributions to Microbiology; Dimorphism in human pathogenic and apathogenic yeasts. print. Publisher: S. Karger AG P. O. Box, CH-4009, Basel, Switzerland. ISSN: 1420-9519. ISBN: 3-8055-6986-6 (cloth).
DOCUMENT TYPE: Book
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 12 OF 27 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2000138362 MEDLINE
DOCUMENT NUMBER: 20138362 PubMed ID: 10672182
TITLE: The cell wall architecture of **Candida albicans** wild-type cells and cell wall-defective mutants.
AUTHOR: Kapteyn J C; Hoyer L L; Hecht J E; Muller W H; Andel A; Verkleij A J; Makarow M; Van Den Ende H; Klis F M
CORPORATE SOURCE: Swammerdam Institute of Life Sciences, University of Amsterdam, Kruislaan 318, 1098 SM Amsterdam, The Netherlands.. kapteyn@bio.uva.nl
CONTRACT NUMBER: AI39441 (NIAID)
SOURCE: MOLECULAR MICROBIOLOGY, (2000 Feb) 35 (3) 601-11. Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407

Last Updated on STN: 20000407
Entered Medline: 20000328

AB In **Candida albicans** wild-type cells, the beta1, 6-glucanase-extractable glycosylphosphatidylinositol (GPI)-dependent cell wall proteins (CWPs) account for about 88% of all covalently linked CWPs. Approximately 90% of these GPI-CWPs, including **Als1p** and Als3p, are attached via beta1,6-glucan to beta1,3-glucan. The remaining GPI-CWPs are linked through beta1,6-glucan to chitin. The beta1,6-glucanase-resistant protein fraction is small and consists of Pir-related CWPs, which are attached to beta1,3-glucan through an alkali-labile linkage. Immunogold labelling and Western analysis, using an antiserum directed against Saccharomyces cerevisiae Pir2p/Hsp150, point to the localization of at least two differentially expressed Pir2 homologues in the cell wall of C. **albicans**. In mnn9Delta and pmt1Delta mutant strains, which are defective in N- and O-glycosylation of proteins respectively, we observed enhanced chitin levels together with an increased coupling of GPI-CWPs through beta1,6-glucan to chitin. In these cells, the level of Pir-CWPs was slightly upregulated. A slightly increased incorporation of Pir proteins was also observed in a beta1, 6-glucan-deficient hemizygous kre6Delta mutant. Taken together, these observations show that C. **albicans** follows the same basic rules as S. cerevisiae in constructing a cell wall and indicate that a cell wall salvage mechanism is activated when **Candida** cells are confronted with cell wall weakening.

L4 ANSWER 13 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:12896 BIOSIS
DOCUMENT NUMBER: PREV200100012896
TITLE: Use of site-directed mutagenesis (SDM) to identify the endothelial cell-binding region of the **Candida albicans ALS1** gene product.
AUTHOR(S): Loza, L., Jr. (1); Filler, S. G. (1); Edwards, J. E., Jr. (1); Fu, Y. (1)
CORPORATE SOURCE: (1) Harbo-UCLA Res. and Ed. Inst., Torrance, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 397. print.
Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 14 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:12894 BIOSIS
DOCUMENT NUMBER: PREV200100012894
TITLE: **Candida albicans ALS1** encodes an adhesin that regulates hyphal formation downstream of EFG1.
AUTHOR(S): Sheppard, D. C. (1); Fu, Y. (1); Ibrahim, A. S. (1); Filler, S. G. (1); Edwards, J. E., Jr. (1)
CORPORATE SOURCE: (1) Harbor-UCLA Res. and Ed. Inst., Torrance, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol.

40, pp. 395. print.
Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 15 OF 27 MEDLINE
ACCESSION NUMBER: 2001334595 MEDLINE
DOCUMENT NUMBER: 21220731 PubMed ID: 11320469
TITLE: **Candida albicans** colonization of surface-sealed interim soft liners.
AUTHOR: Olan-Rodriguez L; Minah G E; Driscoll C F
CORPORATE SOURCE: Advanced Education Program in Prosthodontics, Department of Restorative Dentistry, University of Maryland, Baltimore, MD, USA.
SOURCE: JOURNAL OF PROSTHODONTICS, (2000 Dec) 9 (4) 184-8. Journal code: 9301275. ISSN: 1059-941X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816

AB PURPOSE: This in-vivo investigation evaluated the effect of 2 denture sealer agents on the microbial colonization of a newly placed soft interim denture liner during a period of 14 days. MATERIALS AND METHODS: An interim soft denture liner (Coe-Soft; GC America, **Alsip**, IL) was coated with 2 different denture surface sealants (Palaseal [Heraeus Kulzer, Irvine, CA] and Mono-Poly [Plastodent, New York, NY]). Three rectangular wells of 1 cm wide x 2 cm long x 2 mm deep were placed in the intaglio of 10 maxillary complete dentures and filled with the soft liner material. The soft liner surface was treated with Palaseal (first well) and Mono-Poly (second well), and the unsealed (third well) was used as a control. These were exposed to the oral cavity for 14 days. The effect the sealant had in the prevention of Candidal colonization in vivo of the soft liner material was evaluated. Microbiological specimens were recovered from all samples and cultivated. Microbiological data from the control and 2-test samples in each denture were tabulated, and statistical analyses were performed. RESULTS: This investigation showed clear differences ($p < .001$) between the sealed and unsealed soft liners. The sealed material showed significantly less colonization by yeast and bacteria. Intercomparison of the surface denture sealers, Palaseal versus Mono-Poly, showed no statistically significant differences ($p < .005$) in total yeast or bacterial colonization. CONCLUSION: Coating of Coe-Soft denture liner with either Palaseal or Mono-Poly significantly decreased yeast and bacterial colonization. .

L4 ANSWER 16 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:347134 BIOSIS
DOCUMENT NUMBER: PREV200000347134
TITLE: Characterization of **Candida**

albicans gene, Ala1(Als5) and its protein.
AUTHOR(S): Byrd-Williams, P. B. (1); Gaur, N. K. (1); Klotz, S. A. (1); Henderson, R. L. (1); Moore, M. L. (1)
CORPORATE SOURCE: (1) VA Medical Center, Kansas City, MO USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2000) Vol. 100, pp. 73-74. print.
Meeting Info.: 100th General Meeting of the American Society for Microbiology Los Angeles, California, USA May 21-25, 2000 American Society for Microbiology . ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 17 OF 27 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 2000253093 MEDLINE
DOCUMENT NUMBER: 20253093 PubMed ID: 10790384
TITLE: TUP1, CPH1 and EFG1 make independent contributions to filamentation in **candida albicans**
.
AUTHOR: Braun B R; Johnson A D
CORPORATE SOURCE: Department of Microbiology, University of California, San Francisco, California 94143-0414, USA.
CONTRACT NUMBER: GM-37049 (NIGMS)
SOURCE: GENETICS, (2000 May) 155 (1) 57-67.
Journal code: 0374636. ISSN: 0016-6731.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000720
Last Updated on STN: 20000720
Entered Medline: 20000711

AB The common fungal pathogen, **Candida albicans**, can grow either as single cells or as filaments (hyphae), depending on environmental conditions. Several transcriptional regulators have been identified as having key roles in controlling filamentous growth, including the products of the TUP1, CPH1, and EFG1 genes. We show, through a set of single, double, and triple mutants, that these genes act in an additive fashion to control filamentous growth, suggesting that each gene represents a separate pathway of control. We also show that environmentally induced filamentous growth can occur even in the absence of all three of these genes, providing evidence for a fourth regulatory pathway. Expression of a collection of structural genes associated with filamentous growth, including HYR1, ECE1, HWP1, **ALS1**, and CHS2, was monitored in strains lacking each combination of TUP1, EFG1, and CPH1. Different patterns of expression were observed among these target genes, supporting the hypothesis that these three regulatory proteins engage in a network of individual connections to downstream genes and arguing against a model whereby the target genes are regulated through a central filamentous growth pathway. The results suggest the existence of several distinct types of filamentous forms of C. **albicans**, each dependent on a particular set of environmental conditions and each expressing a unique set of surface proteins.

L4 ANSWER 18 OF 27 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1999346221 MEDLINE
DOCUMENT NUMBER: 99346221 PubMed ID: 10417199
TITLE: Detection of Als proteins on the cell wall of **Candida albicans** in murine tissues.
AUTHOR: Hoyer L L; Clevenger J; Hecht J E; Ehrhart E J; Poulet F M
CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Illinois, Urbana, Illinois, USA.. lhoyer@uiuc.edu
CONTRACT NUMBER: AI39441 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (1999 Aug) 67 (8) 4251-5. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990820
Last Updated on STN: 19990820
Entered Medline: 19990812

AB A murine model of disseminated candidiasis was utilized to determine whether **Candida albicans** Als proteins are produced in vivo. The kidneys, spleen, heart, liver, and lungs were collected from mice inoculated with one of three C. **albicans** strains (SC5314, B311, or WO-1). Immunohistochemical analysis of murine tissues by using a rabbit polyclonal anti-Als serum indicated that Als proteins were produced by each C. **albicans** cell in the tissues examined. Patterns of staining with the anti-Als serum were similar among the C. **albicans** strains tested. These data indicated that Als protein production was widespread in disseminated candidiasis and that, despite strain differences in ALS gene expression previously noted in vitro, Als protein production in vivo was similar among C. **albicans** strains. The extensive production of Als proteins in vivo and their presence on the C. **albicans** cell wall position these proteins well for a role in host-pathogen interaction.

L4 ANSWER 19 OF 27 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 1999390319 MEDLINE
DOCUMENT NUMBER: 99390319 PubMed ID: 10458989
TITLE: Adhesins in **Candida albicans**.
AUTHOR: Sundstrom P
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, Ohio State University, Columbus, OH 43210-1239, USA.. sundstrom.1@osu.edu
SOURCE: CURRENT OPINION IN MICROBIOLOGY, (1999 Aug) 2 (4) 353-7. Ref: 35
Journal code: 9815056. ISSN: 1369-5274.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 19990925

Entered Medline: 19990915

AB The adherent properties of **Candida albicans** blastoconidia and germ tubes have long been appreciated, but little is known about the mechanisms responsible for adherence. Recently, three genes, ALA1, **ALS1** and HWP1, encoding proteins with adherent properties and motifs consistent with linkage to the beta-1, 6-glucan of C. **albicans** cell walls have provided insight into the topology of protein adhesins. Hwp1, a developmentally regulated adhesin of germ tubes and hyphae, attaches to buccal epithelial cells by an unconventional, transglutaminase-mediated mechanism of adhesion.

L4 ANSWER 20 OF 27 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 1998361950 MEDLINE
DOCUMENT NUMBER: 98361950 PubMed ID: 9694829
TITLE: Multiple functions of Pmt1p-mediated protein O-mannosylation in the fungal pathogen **Candida albicans**.
AUTHOR: Timpel C; Strahl-Bolsinger S; Ziegelbauer K; Ernst J F
CORPORATE SOURCE: Institut fur Mikrobiologie und Biologisch-Medizinisches Forschungszentrum, Heinrich-Heine-Universitat, D-40225 Dusseldorf, Germany.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Aug 14) 273 (33) 20837-46.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF000232
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980925
Last Updated on STN: 19980925
Entered Medline: 19980914

AB Protein mannosylation by Pmt proteins initiates O-glycosylation in fungi. We have identified the PMT1 gene and analyzed the function of Pmt1p in the fungal human pathogen **Candida albicans**. Mutants defective in PMT1 alleles lacked Pmt in vitro enzymatic activity, showed reduced growth rates, and tended to form cellular aggregates. In addition, multiple specific deficiencies not known in Saccharomyces cerevisiae (including defective hyphal morphogenesis; supersensitivity to the antifungal agents hygromycin B, G418, clotrimazole, and calcofluor white; and reduced adherence to Caco-2 epithelial cells) were observed in pmt1 mutants. PMT1 deficiency also led to faster electrophoretic mobility of the **Als1p** cell wall protein and to elevated extracellular activities of chitinase. Homozygous pmt1 mutants were avirulent in a mouse model of systemic infection, while heterozygous PMT1/pmt1 strains showed reduced virulence. The results indicate that protein O-mannosylation by Pmt proteins occurs in different fungal species, where PMT1 deficiency can lead to defects in multiple cellular functions.

L4 ANSWER 21 OF 27 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 1998440424 MEDLINE
DOCUMENT NUMBER: 98440424 PubMed ID: 9765564
TITLE: Identification of **Candida albicans**

ALS2 and ALS4 and localization of als proteins to the fungal cell surface.
AUTHOR: Hoyer L L; Payne T L; Hecht J E
CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Illinois, Urbana, Illinois, USA. lhoyer@uiuc.edu
CONTRACT NUMBER: AI39441 (NIAID)
SOURCE: JOURNAL OF BACTERIOLOGY, (1998 Oct) 180 (20) 5334-43. Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF024580; GENBANK-AF024581; GENBANK-AF024582; GENBANK-AF024583; GENBANK-AF024584; GENBANK-AF024585; GENBANK-AF024586; GENBANK-AF024587
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 20000303
Entered Medline: 19981030

AB Additional genes in the growing ALS family of **Candida albicans** were isolated by PCR screening of a genomic fosmid library with primers designed from the consensus tandem-repeat sequence of **ALS1**. This procedure yielded fosmids encoding ALS2 and ALS4. ALS2 and ALS4 conformed to the three-domain structure of ALS genes, which consists of a central domain of tandemly repeated copies of a 108-bp motif, an upstream domain of highly conserved sequences, and a domain of divergent sequences 3' of the tandem repeats. Alignment of five predicted Als protein sequences indicated conservation of N- and C-terminal hydrophobic regions which have the hallmarks of secretory signal sequences and glycosylphosphatidylinositol addition sites, respectively. Heterologous expression of an N-terminal fragment of **Als1p** in Saccharomyces cerevisiae demonstrated function of the putative signal sequence with cleavage following Ala17. This signal sequence cleavage site was conserved in the four other Als proteins analyzed, suggesting identical processing of each protein. Primary-structure features of the five Als proteins suggested a cell-surface localization, which was confirmed by indirect immunofluorescence with an anti-Als antiserum. Staining was observed on mother yeasts and germ tubes, although the intensity of staining on the mother yeast decreased with elongation of the germ tube. Similar to other ALS genes, ALS2 and ALS4 were differentially regulated. ALS4 expression was correlated with the growth phase of the culture; ALS2 expression was not observed under many different in vitro growth conditions. The data presented here demonstrate that ALS genes encode cell-surface proteins and support the conclusion that the size and number of Als proteins on the C. **albicans** cell surface vary with strain and growth conditions.

L4 ANSWER 22 OF 27 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 1998187963 MEDLINE
DOCUMENT NUMBER: 98187963 PubMed ID: 9529114
TITLE: Expression of the **Candida albicans** gene **ALS1** in Saccharomyces cerevisiae induces adherence to endothelial and epithelial cells.
AUTHOR: Fu Y; Rieg G; Fonzi W A; Belanger P H; Edwards J E Jr; Filler S G

CORPORATE SOURCE: St. John's Cardiovascular Research Center, Department of Medicine, Harbor-UCLA Research and Education Institute, Torrance, California 90502, USA.
CONTRACT NUMBER: P01 AI-37194 (NIAID)
R01AI-19990 (NIAID)
R29 AI040636 (NIAID)
+
SOURCE: INFECTION AND IMMUNITY, (1998 Apr) 66 (4) 1783-6. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980416
Last Updated on STN: 19980416
Entered Medline: 19980409

AB To identify genes encoding adhesins that mediate the binding of **Candida albicans** to endothelial cells, a genomic library from this organism was constructed and used to transform Saccharomyces cerevisiae. These transformed organisms were screened for adherence to endothelial cells, and a highly adherent clone was identified. The adherence of this clone to endothelial cells was over 100-fold greater than that of control S. cerevisiae transformed with the empty plasmid. This clone also exhibited enhanced adherence to epithelial cells. The C. **albicans** gene contained within this clone was found to be **ALS1**. These results indicate that **ALS1** may encode a candidal adhesin.

L4 ANSWER 23 OF 27 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 1998309840 MEDLINE
DOCUMENT NUMBER: 98309840 PubMed ID: 9644209
TITLE: **Candida albicans** ALS3 and insights into the nature of the ALS gene family.
AUTHOR: Hoyer L L; Payne T L; Bell M; Myers A M; Scherer S
CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Illinois at Urbana-Champaign, 2522 VMBSB, 2001 S. Lincoln Avenue, Urbana, IL 61802, USA..
lhoyer@uiuc.edu
CONTRACT NUMBER: AI23850 (NIAID)
AI39441 (NIAID)
SOURCE: CURRENT GENETICS, (1998 Jun) 33 (6) 451-9. Journal code: 8004904. ISSN: 0172-8083.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U87956
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980828
Last Updated on STN: 20000303
Entered Medline: 19980814

AB The **ALS1** (**agglutinin-like** sequence) gene of **Candida albicans** encodes a protein similar to alpha-**agglutinin**, a cell-surface adhesion glycoprotein of Saccharomyces cerevisiae (Hoyer et al. 1995). A central domain of a tandemly repeated 108-bp sequence is found in the **ALS1** coding region. This tandem-repeat motif

hybridizes to multiple C. **albicans** genomic DNA fragments, indicating the possibility of other **ALS1**-like genes in C. **albicans** (Hoyer et al. 1995). To determine if these fragments constitute a gene family, tandem-repeat-hybridizing genomic fragments were isolated from a fosmid library by PCR screening using primers based on the consensus tandem-repeat sequence of **ALS1** (Hoyer et al. 1995). One group of fosmids, designated ALS3, encodes a gene with 81% identity to **ALS1**. The sequences of **ALS1** and ALS3 are most conserved in the tandem-repeat domain and in the region 5' of the tandem repeats. Northern-blot analysis using unique probes from the 3' end of each gene demonstrated that **ALS1** expression varies, depending on which C. **albicans** strain is examined, and that ALS3 is hyphal-specific. Both genes are found in a variety of C. **albicans** and C. stellatoidea strains examined. The predicted **Als1p** and Als3p exhibit features suggesting that both are cell-surface glycoproteins. Southern blots probed with conserved sequences from the region 5' of the tandem repeats suggest that other **ALS**-like sequences are present in the C. **albicans** genome and that the **ALS** family may be larger than originally estimated.

L4 ANSWER 24 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:416768 BIOSIS
DOCUMENT NUMBER: PREV199800416768
TITLE: Allelic frequencies and associations in **Candida albicans**.
AUTHOR(S): Lott, T. J.; Holloway, B. P.; Elie, C. M.; Logan, D.
CORPORATE SOURCE: CDC, Atlanta, GA USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1998) Vol. 98, pp. 259. Meeting Info.: 98th General Meeting of the American Society for Microbiology Atlanta, Georgia, USA May 17-21, 1998 American Society for Microbiology . ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English

L4 ANSWER 25 OF 27 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 1998053977 MEDLINE
DOCUMENT NUMBER: 98053977 PubMed ID: 9393828
TITLE: Expression, cloning, and characterization of a **Candida albicans** gene, ALA1, that confers adherence properties upon Saccharomyces cerevisiae for extracellular matrix proteins.
AUTHOR: Gaur N K; Klotz S A
CORPORATE SOURCE: Research Service, Veterans Affairs Medical Center, Kansas City, Missouri 64128, USA.
SOURCE: INFECTION AND IMMUNITY, (1997 Dec) 65 (12) 5289-94. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF025429
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980122
Last Updated on STN: 20000303

Entered Medline: 19980102

AB Adherence of **Candida albicans** to host tissues is a necessary step for maintenance of its commensal status and is likely a necessary step in the pathogenesis of candidiasis. The extracellular matrix (ECM) proteins are some of the host tissue and plasma proteins to which C. **albicans** adheres through adhesins located on the fungal cell surface. To isolate genes encoding ECM adhesins, an assay was developed based on the ability of yeast cells to adhere to magnetic beads coated with the ECM protein fibronectin, type IV collagen, or laminin. A C. **albicans** genomic library was constructed by cloning XbaI-partially-digested and size-selected fragments into pAUR112, an Escherichia coli-yeast low-copy-number shuttle vector. The C. **albicans** library was transformed into Saccharomyces cerevisiae YPH 499, and clones capable of adherence were selected by using ECM protein-coated magnetic beads. A plasmid containing an approximately 8-kb insert was isolated from 29 adherent clones. These clones exhibited adherence to all ECM protein-coated magnetic beads and to human buccal epithelial cells. The ALA1 gene (for **agglutinin-like** adhesin) was localized by subcloning it into a 5-kb XbaI fragment which retained the adherence phenotype in both orientations. The complete DNA sequence of the 5-kb insert was determined, and an open reading frame (ORF) encoding 1,419 amino acid residues was identified. Deletions from the 5' and 3' ends extending into the DNA sequence encoding the 1,419-amino-acid ORF product inactivated the adherence phenotype, suggesting that it is the coding region of the ALA1 gene. A database search identified ALA1 to be similar to the C. **albicans** **ALS1** (for **agglutinin-like** sequence 1) protein and the S. cerevisiae agglutinin protein (AG alpha1), although the homology at the primary amino acid sequence level is limited to the first half of each of these proteins. ALA1 contains a central domain of six tandem repeats of 36 amino acids. We discuss the significance of various predicted ALA1 structural motifs and their relationships to function in the adherence process.

L4 ANSWER 26 OF 27 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 95272392 MEDLINE
DOCUMENT NUMBER: 95272392 PubMed ID: 7752895
TITLE: **Candida albicans ALS1**: domains related to a Saccharomyces cerevisiae sexual agglutinin separated by a repeating motif.
AUTHOR: Hoyer L L; Scherer S; Shatzman A R; Livi G P
CORPORATE SOURCE: Human Genome Center, Lawrence Berkeley Laboratory, Berkeley, California 94720.
CONTRACT NUMBER: AI23850 (NIAID)
SOURCE: MOLECULAR MICROBIOLOGY, (1995 Jan) 15 (1) 39-54. Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L25902
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950629
Last Updated on STN: 19950629
Entered Medline: 19950621

AB Transfer of budding **Candida albicans** yeast cells

from the rich, complex medium YEPD to the defined tissue culture medium RPMI 1640 (RPMI) at 37 degrees C and 5% CO2 causes rapid onset of hyphal induction. Among the genes induced under these conditions are hyphal-specific genes as well as genes expressed in response to changes in temperature, CO2 and specific media components. A cDNA library constructed from cells incubated for 20 min in RPMI was differentially screened with yeast (YEPD)- and hyphal (RPMI)-specific probes resulting in identification of a gene expressed in response to culture conditions but not regulated by the yeast-hyphal transition. The deduced gene product displays significant identity to Saccharomyces cerevisiae alpha-agglutinin, encoded by AG alpha 1, an adhesion glycoprotein that mediates mating of haploid cells. The presence of this gene in C. **albicans** is curious since the organism has not been observed to undergo meiosis. We designate the C. **albicans** gene **ALS1** (for **agglutinin-like** sequence). While the N- and C-termini of the predicted 1260-amino-acid **ALS1** protein resemble those of the 650-amino-acid AG alpha 1, **ALS1** contains a central domain of tandem repeats consisting of a highly conserved 36-amino-acid sequence not present in AG alpha 1. These repeats are also present on the nucleotide level as a highly conserved 108 bp motif. Southern and Northern blot analyses indicate a family of C. **albicans** genes that contain the tandem repeat motif; at least one gene in addition to **ALS1** is expressed under conditions similar to those for **ALS1** expression. Genomic Southern blots from several C. **albicans** isolates indicate that the number of copies of the tandem repeat element in **ALS1** differs across strains and, in some cases, between **ALS1** alleles in the same strain, suggesting a strain-dependent variability in **ALS1** protein size. Potential roles for the **ALS1** protein are discussed.

L4 ANSWER 27 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1978:136611 BIOSIS
DOCUMENT NUMBER: BA65:23611
TITLE: PERCURRENT PROLIFERATION OF SPORANGIOPHORES IN THE GENUS ALBUGO.
AUTHOR(S): THAKUR S B
CORPORATE SOURCE: DEP. BOT., RUPAREL COLL., BOMBAY 400016, MAHARASHTRA, INDIA.
SOURCE: MYCOLOGIA, (1977) 69 (3), 637-641.
CODEN: MYCOAE. ISSN: 0027-5514.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Sporangiogenesis in 5 spp. of Albugo is described. A. bliti (Biv.) Kuntze, A. **candida** (Pers.) Kuntze, A. evolvuli (Damle) Safee. & Thirum., A. ipomoeae-aquaticae Sawada and A. pestigridis Gharse occurring on Amaranthus polygamus L. along with Raphanus sativus L., Evolvulus **alsinoides** Roxb., Ipomoea aquatica Forsk., and I. pestigridis L., respectively, were used for this study. The sporangia of Albugo spp. apparently are aleuriosporangia and the sporangiophores are annellosporangiophores.

(FILE HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, TOXCENTER, PHIC, PHIN' ENTERED AT 09:55:39 ON 07 OCT 2002)
L5 11711 S EDWARDS J?/AU
L6 23 S "FILER S"?/AU
L7 1331 S CUTLER J?/AU

Author(s)

L8	1501	S SHEPPARD D?/AU
L9	2403	S IBRAHIM A?/AU
L10	5724	S FU Y?/AU
L11	250	S "FILLER S"?/AU
L12	4	S L5 AND (L6 OR L11) AND L7 AND L8 AND L9 AND L10
L13	168	S L5 AND (L6 OR L11 OR L7 OR L8 OR L9 OR L10)
L14	60	S (L6 OR L11) AND (L7 OR L8 OR L9 OR L10)
L15	4	S L7 AND (L8 OR L9 OR L10)
L16	8	S L8 AND (L9 OR L10)
L17	44	S L9 AND L10
L18	11	S (L13 OR L14 OR L17) AND L1
L19	13	S L12 OR L15 OR L16 OR L18
L20	7	DUP REM L19 (6 DUPLICATES REMOVED)

L20 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1

ACCESSION NUMBER: 2002:355852 HCAPLUS
DOCUMENT NUMBER: 137:90678
TITLE: Candida albicans **Als1p**: An adhesin that is a downstream effector of the EFG1 filamentation pathway
AUTHOR(S): **Fu, Yue**; **Ibrahim, Ashraf S.**; **Sheppard, Donald C.**; Chen, Yee-Chun; French, Samuel W.; **Cutler, Jim E.**; **Filler, Scott G.**; **Edwards, John E., Jr.**
CORPORATE SOURCE: Division of Infectious Diseases, St John's Cardiovascular Research Center, Harbor-UCLA Research and Education Institute, Torrance, CA, 90502, USA
SOURCE: Molecular Microbiology (2002), 44(1), 61-72
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Filamentation and adherence to host cells are crit. virulence factors of Candida albicans. Multiple filamentation regulatory pathways have been discovered in C. albicans using Saccharomyces cerevisiae as a model. In S. cerevisiae, these pathways converge on Flo11p, which functions as a downstream effector of filamentation and also mediates cell-cell adherence (flocculation). In C. albicans, such effector(s) have not yet been identified. Here, we demonstrate that the cell surface protein **Als1p** is an effector of filamentation in C. albicans. We show that **Als1p** expression is controlled by the transcription factor Efg1p, which is known to be a key regulator of filamentation in C. albicans. Further, disruption of **ALS1** inhibited filamentation, and autonomous expression of **Als1p** restored filamentation in an efg1 homozygous null mutant. Thus, **Als1p** functions as a downstream effector of the EFG1 filamentation pathway. In addn., we found that **Als1p** mediates both flocculation and adherence of C. albicans to endothelial cells in vitro. As a cell surface glycoprotein that mediates filamentation and adherence, **Als1p** has both structural and functional similarity to S. cerevisiae Flo11p. Consistent with our in vitro results, **Als1p** was required for both normal filamentation and virulence in the mouse model of hematogenously disseminated candidiasis.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE

FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:486908 BIOSIS
DOCUMENT NUMBER: PREV200200486908
TITLE: A functional analysis of the ALS5, ALS6 and ALS7 genes of Candida albicans.
AUTHOR(S): **Sheppard, D. C. (1); Ibrahim, A. S. (1); Fu, Y. (1)**; Filler, S. G. (1); Edwards, J. E., Jr. (1)
CORPORATE SOURCE: (1) Division of Infectious Diseases, Harbor-UCLA Research and Education Institute, Torrance, CA USA
SOURCE: International Journal of Infectious Diseases, (June, 2002) Vol. 6, No. Supplement 2, pp. 2S52-2S53. http://www.isid.org/publications/ijid.shtml. print. Meeting Info.: 12th International symposium on infections in the immunocompromised host Bergen, Norway June 23-26, 2002 International Immunocompromised Host Society . ISSN: 1201-9712.
DOCUMENT TYPE: Conference
LANGUAGE: English

L20 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:486896 BIOSIS
DOCUMENT NUMBER: PREV200200486896
TITLE: Expression analysis of **Agglutinin-Like** Sequence 1 of Candida albicans.
AUTHOR(S): **Ibrahim, A. S. (1); Sheppard, D. C. (1); Fu, Y. (1); Edwards, J. E., Jr. (1)**
CORPORATE SOURCE: (1) Harbor-UCLA Research and Education Institute, Torrance, CA USA
SOURCE: International Journal of Infectious Diseases, (June, 2002) Vol. 6, No. Supplement 2, pp. 2S47. http://www.isid.org/publications/ijid.shtml. print. Meeting Info.: 12th International symposium on infections in the immunocompromised host Bergen, Norway June 23-26, 2002 International Immunocompromised Host Society . ISSN: 1201-9712.
DOCUMENT TYPE: Conference
LANGUAGE: English

L20 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:223311 BIOSIS
DOCUMENT NUMBER: PREV200200223311
TITLE: The chromosomal location of EFG1 has a major impact on the morphology and virulence of Candida albicans.
AUTHOR(S): **Sheppard, D. C. (1); Ibrahim, A. S. (1); Fu, Y. (1)**; Edwards, J. E. (1); Filler, S. G. (1)
CORPORATE SOURCE: (1) Harbor-UCLA Research and Education Institute, Torrance, CA USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 364. http://www.asmusa.org/mtgsrc/generalmeeting.htm.

print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001
ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Candida albicans strains containing disruptions in both copies of the gene encoding the transcription factor EFG1 have markedly impaired hyphal production, a reduced capacity to cause endothelial cell injury and attenuated virulence. Re-introduction of a single copy of EFG1 into the LEU2 locus of the efg1/efg1 strain only partially reconstitutes the wild-type phenotype. We investigated the relative contribution of gene locus to this phenomenon by constructing multiple strains in which a wild-type allele of EFG1 and its promoter were integrated at different loci. The allele was introduced into the efg1/efg1 strain at either the native (EFG1) locus, or one of two non-native loci: LEU2 or ARG4. Integration of EFG1 at the native locus resulted in complete reconstitution of filamentation with abundant hyphae formation in response to serum. However, strains containing EFG1 at either of the non-native loci formed only pseudohyphae under these conditions. Similarly, integration of EFG1 at the native locus restored the ability to induce endothelial cell damage to wild-type levels, while the strains containing EFG1 at the LEU2 or ARG4 loci caused markedly less endothelial damage (45% and 100% reduction in damage compared with wild-type, $p>0.001$). Finally, when studied in the mouse model of hematogenous candidiasis, the strain containing EFG1 at the native locus was as virulent as wild-type C. albicans. In contrast, the strains in which EFG1 was introduced at the LEU2 or ARG4 loci displayed significantly attenuated virulence. Northern blot analysis demonstrated reduced expression of an abnormally small EFG1 transcript in the strains containing EFG1 at the non-native loci. Thus, in C. albicans, the locus of integration is critical in studying gene function, and can result in significant alterations in phenotype both in vitro and in vivo.

L20 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:12896 BIOSIS
DOCUMENT NUMBER: PREV200100012896
TITLE: Use of site-directed mutagenesis (SDM) to identify the endothelial cell-binding region of the Candida albicans **ALS1** gene product.
AUTHOR(S): Loza, L., Jr. (1); **Filler, S. G. (1)**; **Edwards, J. E., Jr. (1)**; **Fu, Y. (1)**
CORPORATE SOURCE: (1) Harbo-UCLA Res. and Ed. Inst., Torrance, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 397. print.
Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L20 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:12894 BIOSIS

DOCUMENT NUMBER: PREV200100012894
TITLE: Candida albicans **ALS1** encodes an adhesin that regulates hyphal formation downstream of EFG1.
AUTHOR(S): **Sheppard, D. C. (1); Fu, Y. (1); Ibrahim, A. S. (1); Filler, S. G. (1) ; Edwards, J. E., Jr. (1)**
CORPORATE SOURCE: (1) Harbor-UCLA Res. and Ed. Inst., Torrance, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 395. print.
Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L20 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 1998:214170 HCAPLUS
DOCUMENT NUMBER: 128:320030
TITLE: Expression of the Candida albicans gene **ALS1** in Saccharomyces cerevisiae induces adherence to endothelial and epithelial cells
AUTHOR(S): **Fu, Yue**; Rieg, Gunter; Fonzi, William A.; Belanger, Paul H.; **Edwards, John E., Jr.**; **Filler, Scott G.**
CORPORATE SOURCE: St. John's Cardiovascular Research Center, Division of Infectious Diseases, Department of Medicine, Harbor-UCLA Research and Education Institute, Torrance, CA, 90502, USA
SOURCE: Infection and Immunity (1998), 66(4), 1783-1786
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To identify genes encoding adhesins that mediate the binding of Candida albicans to endothelial cells, a genomic library from this organism was constructed and used to transform Saccharomyces cerevisiae. These transformed organisms were screened for adherence to endothelial cells, and a highly adherent clone was identified. The adherence of this clone to endothelial cells was over 100-fold greater than that of control S. cerevisiae transformed with the empty plasmid. This clone also exhibited enhanced adherence to epithelial cells. The C. albicans gene contained within this clone was **ALS1**. These results indicate that **ALS1** may encode a candidal adhesin.

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, TOXCENTER, PHIC, PHIN' ENTERED AT 10:52:24 ON 07 OCT 2002)
L21 15 S (L5 OR L6 OR L11 OR L7 OR L8 OR L9 OR L10) AND L1
L22 4 S L21 NOT L19
L23 1 DUP REM L22 (3 DUPLICATES REMOVED)

L23 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:639230 HCAPLUS
TITLE: Contribution of Candida albicans **ALS1** to the pathogenesis of experimental oropharyngeal candidiasis

AUTHOR(S): Kamai, Yasuki; Kubota, Mikie; Kamai, Yoko; Hosokawa, Tsunemichi; Fukuoka, Takashi; **Filler, Scott G.**

CORPORATE SOURCE: Biological Research Laboratories, Sankyo Co., Ltd., Tokyo, 140-8710, Japan

SOURCE: Infection and Immunity (2002), 70(9), 5256-5258
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We investigated the contribution of Candida albicans **ALS1**, which encodes a candidal adhesin, to the pathogenesis of exptl. murine oropharyngeal candidiasis. Our results indicate that the **ALS1** gene product is important for the adherence of the organism to the oral mucosa during the early stage of the infection.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'HOME' ENTERED AT 10:56:33 ON 07 OCT 2002

Devi, S.
09/715876

07oct02 09:45:04 User219783 Session D1873.1

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key terms

Set Items Description
S1 2914 ALSI? OR ALS1? OR ALS(10N)AGGLUTIN? OR AGGLUTIN?(W)LIKE
S2 37 S1 AND (CANDIDA OR ALBICANS OR KRUSEI OR TROPICALIS OR PARAPSILOS?)
S3 24 RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113

3/3,AB/1 (Item 1 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online
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01870550 AADAAI1406782
The identification of the endothelial-cell binding region of the *Candida"** *albicans"** *ALS1"** gene product
Author: Loza, Lucio, Jr.
Degree: M.S.
Year: 2001
Corporate Source/Institution: California State University, Dominguez Hills (0582)
Source: VOLUME 40/03 of MASTERS ABSTRACTS.
PAGE 653. 58 PAGES
ISBN: 0-493-41706-0

italic>*Candida"** *albicans"**</italic> causes serious infections in immunocompromised patients. These blood-borne organisms adhere to the endothelial cell lining of the blood vessels subsequently escaping and invading the deep tissues. This study investigated the mechanisms by which <italic>*Candida"** *albicans"**</italic> adheres to vascular endothelial cells in vitro.

The specific aim of this project is to identify the endothelial cell-binding region of the candidal adhesion gene product, *Als1p"**. This was accomplished by constructing mutants of <italic>*ALS1"**</italic> through the use of site-directed mutagenesis. The mutant constructs were

transformed to the normally non-adhering <italic> S. cerevisiae</italic>. The adherence of the transformants was determined and compared to <italic>S. cerevisiae</italic> expressing the wild type *Als1p"**. The binding region of *Als1p"** is likely within the region of the N-terminus corresponding to amino acids 278 through 287. This study also determined that the presence of the tandem repeats of *Als1p"** might contribute to its function as an adhesin.

3/3,AB/2 (Item 2 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online

01781048 AADAAIMQ49128
Identification de genes potentiellement impliques dans le dimorphisme cellulaire de *Candida"** *albicans"** (French text)
Author: Tremblay, Tammy-Lynn
Degree: M.Sc.
Year: 2000
Corporate Source/Institution: Universite Laval (Canada) (0726)
Source: VOLUME 38/06 of MASTERS ABSTRACTS.
PAGE 1547. 77 PAGES
ISBN: 0-612-49128-5

La capacité de passer d'une forme levure à une forme mycélienne est considérée comme importante dans la pathogénicité de <italic>*Candida"** *albicans"**</italic>. Dans le but d'identifier des gènes potentiellement impliqués dans le contrôle du dimorphisme, l'expression de gènes fut comparée entre des cellules de type levuriforme et des cellules engagées dans la voie mycélienne par la technique du <italic>Differential Display</italic>. Des dix-sept fragments d'ADNc isolés, onze se sont avérés ˆtre exprimés plus intensément dans les cellules engagées dans la voie mycélienne que dans les cellules levuriformes. La séquence nucléotidique fut déterminée pour six de ces fragments d'ADNc. Un seul des six fragments d'ADN identifiés correspondait à un gène de <italic>C. *albicans"**</italic> déjà identifié soit le “<italic> *Candida"** *albicans"** *agglutinin"**-*like"** protein</italic> (ALS3)”. Parmi les cinq autres fragments identifiés, trois possédaient des cadres de lecture ayant une grande similarité avec des protéines de <italic> Sacharomyces cervisiae</italic> la “<italic>probable membrane protein YOR088w</italic>”, une “ARN hélicase ATP-dépendante” et la “<italic>putative phosphate-repressible phosphate permease YBR29C </italic>”. Les deux autres fragments d'ADNc séquencés ne présentaient aucune similarité avec les séquences comprises dans les multiples banques de données.

3/3,AB/3 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

14211617 PASCAL No.: 99-0412210
Adhesins in *Candida"** *albicans"** : Host-microbe interactions: fungi/viruses/parasites

SUNDSTROM P
Department of Medical Microbiology and Immunology, Ohio State University, Columbus, OH 43210-1239, United States
Journal: Current opinion in microbiology, 1999, 2 (4) 353-357
Language: English
The adherent properties of *Candida"** *albicans"** blastoconidia and germ tubes have long been appreciated, but little is known about the mechanisms responsible for adherence. Recently, three genes, ALA1, *ALS1"** and HWP1, encoding proteins with adherent properties and motifs consistent with linkage to the beta -1,6-glucan of C. *albicans"** cell walls have provided insight into the topology of protein adhesins. Hwp1, a developmentally regulated adhesin of germ tubes and hyphae, attaches to buccal epithelial cells by an unconventional, transglutaminase-mediated mechanism of adhesion.

3/3,AB/4 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

13561043 PASCAL No.: 98-0263005
Expression of the *Candida"** *albicans"** gene *ALS1"** in Saccharomyces cerevisiae induces adherence to endothelial and epithelial cells
YUE FU; RIEG G; FONZI W A; BELANGER P H; EDWARDS J E JR; FILLER S G
St. John's Cardiovascular Research Center, Division of Infectious Diseases, Department of Medicine, Harbor-UCLA Research and Education Institute, Torrance, California 90502, United States; Department of Microbiology and Immunology, Georgetown University, Washington, D.C. 20007, United States; UCLA School of Medicine, Los Angeles, California 90024, United States
Journal: Infection and immunity, 1998, 66 (4) 1783-1786
Language: English
To identify genes encoding adhesins that mediate the binding of *Candida"** *albicans"** to endothelial cells, a genomic library from this organism was constructed and used to transform Saccharomyces cerevisiae. These transformed organisms were screened for adherence to endothelial cells, and a highly adherent clone was identified. The adherence of this clone to endothelial cells was over 100-fold greater than that of control S. cerevisiae transformed with the empty plasmid. This clone also exhibited enhanced adherence to epithelial cells. The C. *albicans"** gene contained within this clone was found to be *ALS1"**. These results indicate that *ALS1"** may encode a candidal adhesin.

3/3,AB/5 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

13364238 PASCAL No.: 98-0092620
Expression, cloning, and characterization of a *Candida"** *albicans"** gene, ALA1, that confers adherence properties upon Saccharomyces cerevisiae for extracellular matrix proteins
GAUR N K; KLOTZ S A
Research Service, Veterans Affairs Medical Center, Kansas City, Missouri,

United States; Department of Medicine, University of Kansas School of Medicine, Kansas City, Kansas, United States; Department of Microbiology, University of Kansas School of Medicine, Kansas City, Kansas, United States
Journal: Infection and immunity, 1997, 65 (12) 5289-5294
Language: English
Adherence of *Candida"** *albicans"** to host tissues is a necessary step for maintenance of its commensal status and is likely a necessary step in the pathogenesis of candidiasis. The extracellular matrix (ECM) proteins are some of the host tissue and plasma proteins to which C. *albicans"** adheres through adhesins located on the fungal cell surface. To isolate genes encoding ECM adhesins, an assay was developed based on the ability of yeast cells to adhere to magnetic beads coated with the ECM protein fibronectin, type IV collagen, or laminin. A C. *albicans"** genomic library was constructed by cloning XbaI-partially-digested and size-selected fragments into pAUR112, an Escherichia coli-yeast low-copy-number shuttle vector. The C. *albicans"** library was transformed into Saccharomyces cerevisiae YPH 499, and clones capable of adherence were selected by using ECM protein-coated magnetic beads. A plasmid containing an similar 8-kb insert was isolated from 29 adherent clones. These clones exhibited adherence to all ECM protein-coated magnetic beads and to human buccal epithelial cells. The ALAI gene (for *agglutinin"**-*like"** adhesin) was localized by subcloning it into a 5-kb XbaI fragment which retained the adherence phenotype in both orientations. The complete DNA sequence of the 5-kb insert was determined, and an open reading frame (ORF) encoding 1,419 amino acid residues was identified. Deletions from the 5' and 3' ends extending into the DNA sequence encoding the 1,419-amino-acid ORF product inactivated the adherence phenotype, suggesting that it is the coding region of the ALAI gene. A database search identified ALA1 to be similar to the C. *albicans"** *ALS1"** (for *agglutinin"**-*like"** sequence 1) protein and the S. cerevisiae agglutinin protein (AG alpha 1), although the homology at the primary amino acid sequence level is limited to the first half of each of these proteins. ALA1 contains a central domain of six tandem repeats of 36 amino acids. We discuss the significance of various predicted ALA1 structural motifs and their relationships to function in the adherence process.

3/3,AB/6 (Item 1 from file: 266)
DIALOG(R)File 266:FEDRIP

00294992
IDENTIFYING NO.: 5R01AI37201-07 AGENCY CODE: CRISP
SALMONELLA VACCINES THAT DELIVER BOTH ANTIGEN AND CYTOKINE
PRINCIPAL INVESTIGATOR: HEFFRON, FRED L
ADDRESS: OREGON HEALTH SCIENCE UNIV 3181 SW SAM JACKSON PARK RD PORTLAND, OR 97201-3098
PERFORMING ORG.: OREGON HEALTH & SCIENCE UNIVERSITY, PORTLAND, OREGON
SPONSORING ORG.: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
FY : 2001
SUMMARY: This proposal for a Mycology Research Unit (MRU) is focused on a comprehensive e ffort to identify and evaluate the ability the ability of candidate antigens to produce protective immunity against hematogenously disseminated candidiasis. The driving forces behind this effort are the high frequency of candidal infections , the attractiveness of a future DNA vaccine strategy, and the need for treatmen t approaches that will minimize

the development of antifungal resistance. Projec t 1 builds on the discovery during the current grant period that antibody respon se to certain epitopes of the phosphomannan complex of C. *albicans"** enhances resi stance to experimental disseminated candidiasis. Approaches for the proposed per iod include: i) use of stabilized liposomal constructs to improve the liposomal vaccine formulations, ii) production of protein conjugates of the critical manna n epitopes, and iii) construction of a DNA vaccine based on peptide mimotopes of the "protective" mannan epitopes. Project 2 is based on the central hypothesis that the ASL (agglutinin mimotopes of the "protective" mannan epitopes. Project 2 is based on the central hypothesis that the ASL (*agglutinin"** *like"** sequence) gen e family of *Candida"** contains genes that encode dominant adhesions of *Candida"** for a variety of host constituents. Gene products of the ALS gene family will be ev aluated as potential vaccine targets for both active and passive immunization. T he active immunization will be accomplished using DNA vaccine approaches and may be used in combination with phosphomannan antigens identified in project 1 to o ptimize an immune response. Project 3 will utilize the ability of affinity-purif y large amounts of anti-mannan antibodies from human plasma to directly test the biological activities of these antibodies and the contribution to protection of the fine epitope specificity of human anti-mannan antibody. Project 4 utilizes highly innovative molecular biology strategies to identify yet undiscovered cell surface proteins that may be attractive vaccine targets. Genes that are expres sed during infection will be identified by screening of random fusion genes. Com parison of functional sequences to the C. *albicans"** genomic sequence will permit identification of likely secreted, cell wall, and transmembrane proteins, availa ble for interaction with antibody. These gene products can then be used either a lone or in combination with other target immunogens to develop effective vaccine s. This technology lends itself well to the incorporation of multiple candidate immunogens into DNA vaccines.

3/3,AB/7 (Item 2 from file: 266)
DIALOG(R)File 266:FEDRIP

00294987
IDENTIFYING NO.: 5P01AI37194-07 0001 AGENCY CODE: CRISP
*CANDIDA"** ALS GENE PRODUCTS AS TARGET IMMUNOGENS
PRINCIPAL INVESTIGATOR: EDWARDS, JOHN E., JR
ADDRESS: HARBOR-UCLA RESEARCH & ED INS 1000 W CARSON STREET TORRANCE, CA 90509
PERFORMING ORG.: HARBOR-UCLA RESEARCH & EDUC INST, TORRANCE, CALIFORNIA
SPONSORING ORG.: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
FY : 2001
SUMMARY: While potent antifungal agents exist that are microbicidal for *Candida"** , the attr ibutable mortality of candidemia is approximately 38%, even with currently avail able antifungal therapy. The use of either passive or active immuno-therapy agai nst *Candida"** is a promising alternative to standard anti- fungal therapy of its p otential to avoid the problems association with heavy use of antifungal agents. Our long range goal is to identify dominant candidal adhesions and use these adh esions as targets for active or passive immunotherapy for serious candidal infec tions. During the current project period, we determined that the C. *albicans"** gen e, *ALS1"** , likely encodes an adhesin that mediated attachment to endothelial and e pithelial cells. This gene is a member of the ALS gene family. To date, approxim ately 11 members of the ALS gene

family have been identified. However, the seque nce of only two of these genes have been published. It is our central hypothesis that the ALS gene family encodes the major adhesion of C. *albicans"**. It is likel y that the different ALS proteins mediate adherence to different host constituen t ligands. We propose to systematically examine selected members of the ALS gene family to determine which of them encode adhesins that mediate the binding of C . *albicans"** to endothelium epithelium, and other host constituents. This informat ion will be used to develop techniques to block the adherence of the organism to host tissues by using either passive or active immunization. The Specific Aims for this project are to i) obtain thje full-length sequence of ALS6 and ALS94-98 ; ii) determine if the above ALS genes encode adhesions to endothelial cells, ep ithelial cells and selected other host constituents, and determine the ligands o n the cell surface to which they bind; iii) determine if antibodies against spec ific ALS proteins block the adherence of C. *albicans"** to endothelial and epitheli al cells, and the selected host constituents in vitro; and iv) determine if anti bodies against specific ALS proteins protect mice from mucosal and hematogenousl y disseminated candidal infections. We will identify adhesion as targets for act ive and passive immunization strategies. These adhesins are highly attractive ta rgets for immunotherapy by themselves, have the potential to be used in combinat ion with the targets identified by other projects in the Mycology Research Unit.

3/3,AB/8 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

14529564 Document Delivery Available: 000177491100062 References: 12
TITLE: Contribution of *Candida"** *albicans"** *ALS1"** to the pathogenesis of experimental oropharyngeal candidiasis
AUTHOR(S): Kamai Y (REPRINT); Kubota M; Kamai Y; Hosokawa T; Fukuoka T; Filler SG
AUTHOR(S) E-MAIL: ykamai@shina.sankyo.co.jp
CORPORATE SOURCE: Sankyo Co Ltd, Shinagawa Ku, 2-58 Hiromachi 1 Chome/Tokyo 1408710//Japan/ (REPRINT); Sankyo Co Ltd, Shinagawa Ku, /Tokyo 1408710//Japan/; Sankyo Co Ltd, Shinagawa Ku, /Tokyo 1408710//Japan/; Harbor UCLA Res & Educ Inst, /Torrance//CA/90502
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 2002, V70, N9 (SEP), P5256-5258
GENUINE ARTICLE#: 584WE
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: We investigated the contribution of *Candida"** *albicans"** *ALS1"**, which encodes a candidal adhesin, to the pathogenesis of experimental murine oropharyngeal candidiasis. Our results indicate that the *ALS1"** gene product is important for the adherence of the organism to the oral mucosa during the early stage of the infection.

3/3,AB/9 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

14482585 Document Delivery Available: 000177381800001 References: 51

TITLE: Adhesion in *Candida"** spp
AUTHOR(S): Sundstrom P (REPRINT)
AUTHOR(S) E-MAIL: sundstrom.1@osu.edu
CORPORATE SOURCE: Ohio State Univ, Dept Mol Virol Immunol & Med Genet, /Columbus//OH/43210 (REPRINT); Ohio State Univ, Dept Mol Virol Immunol & Med Genet, /Columbus//OH/43210; Ohio State Univ, Dept Microbiol, /Columbus//OH/43210
PUBLICATION TYPE: JOURNAL
PUBLICATION: CELLULAR MICROBIOLOGY, 2002, V4, N8 (AUG), P461-469
GENUINE ARTICLE#: 582ZV
PUBLISHER: BLACKWELL PUBLISHING LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND
ISSN: 1462-5814
LANGUAGE: English DOCUMENT TYPE: REVIEW

ABSTRACT: Microbial adherence is one of the most important determinants of pathogenesis, yet very few adhesins have been identified from fungal pathogens. Four structurally related adhesins, Hwp1, Ala1p/Als5p, *Als1p"** , from *Candida"** *albicans"** and Epa1p from *Candida"** glabrata , are members of a class of proteins termed glycosylphosphatidylinositol-dependent cell wall proteins (GPI-CWP). These proteins have N-terminal signal peptides and C-terminal features that mediate glycosylphosphatidylinositol (GPI) membrane anchor addition, as well as other determinants leading to attachment to cell wall glucan. While common signalP/GPI motifs facilitate cell surface expression, unique features mediate ligand binding specificities of adhesins. The first glimpse of structural features of putative adhesins has come from biophysical characterizations of the N-terminal domain of Als5p. One protein not in the GPI-CWP class that was initially described as an adhesin, Int1p, has recently been shown to be similar to Bud4p of Saccharomyces cerevisiae in primary amino acid sequence, in co-localizing with septins and in functioning in bud site selection. Progress in understanding the role of adhesins in oroesophageal candidiasis has been made for Hwp1 in a study using beige athymic and transgenic epsilon 26 mice that have combined defects in innate and acquired immune responses. Searches of the C. *albicans"** genome for proteins in the GPI-CWP class has led to the identification of a subset of genes that will be the focus of future efforts to identify new *Candida"** adhesins.

3/3,AB/10 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13808482 Document Delivery Available: 000175052300006 References: 31
TITLE: *Candida"** *albicans"** *Als1p"**: an adhesin that is a downstream effector of the EFG1 filamentation pathway
AUTHOR(S): Fu Y (REPRINT); Ibrahim AS; Sheppard DC; Chen YC; French SW; Cutler JE; Filler SG; Edwards JE
AUTHOR(S) E-MAIL: Yue Fu@humc.edu; Ibrahim@humc.edu
CORPORATE SOURCE: Harbor UCLA Res & Educ Inst, Div Infect Dis, Bldg RB2,1124 W Carson St/Torrance//CA/90502 (REPRINT); Harbor UCLA Res & Educ Inst, Div Infect Dis, /Torrance//CA/90502; Univ Calif Los Angeles, Sch Med, /Los Angeles//CA/90024; Montana State Univ, Dept Microbiol, /Bozeman//MT/59717
PUBLICATION TYPE: JOURNAL
PUBLICATION: MOLECULAR MICROBIOLOGY, 2002, V44, N1 (APR), P61-72
GENUINE ARTICLE#: 542PB

PUBLISHER: BLACKWELL PUBLISHING LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND
ISSN: 0950-382X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Filamentation and adherence to host cells are critical virulence factors of *Candida"** *albicans"** . Multiple filamentation regulatory pathways have been discovered in C. *albicans"** using Saccharomyces cerevisiae as a model. In S. cerevisiae , these pathways converge on Flo11p, which functions as a downstream effector of filamentation and also mediates cell-cell adherence (flocculation). In C. *albicans"** , such effector(s) have not yet been identified. Here, we demonstrate that the cell surface protein *Als1p"** is an effector of filamentation in C. *albicans"** . We show that *Als1p"** expression is controlled by the transcription factor Efg1p, which is known to be a key regulator of filamentation in C. *albicans"** . Further, disruption of *ALS1"** inhibited filamentation, and autonomous expression of *Als1p"** restored filamentation in an efg1 homozygous null mutant. Thus, *Als1p"** functions as a downstream effector of the EFG1 filamentation pathway. In addition, we found that *Als1p"** mediates both flocculation and adherence of C. *albicans"** to endothelial cells in vitro . As a cell surface glycoprotein that mediates filamentation and adherence, *Als1p"** has both structural and functional similarity to S. cerevisiae Flo11p. Consistent with our in vitro results, *Als1p"** was required for both normal filamentation and virulence in the mouse model of haematogenously disseminated candidiasis.

3/3,AB/11 (Item 4 from file: 440)

13018056 References: 49
TITLE: Biofilm formation by the fungal pathogen *Candida"** *albicans"**: Development, architecture, and drug resistance
AUTHOR(S): Chandra J; Kuhn DM; Mukherjee PK; Hoyer LL; McCormick T; Ghannoum MA (REPRINT)
AUTHOR(S) E-MAIL: mag3@po.cwru.edu
CORPORATE SOURCE: Univ Hosp Cleveland, Ctr Med Mycol, 11100 Euclid Ave/Cleveland//OH/44106 (REPRINT); Univ Hosp Cleveland, Ctr Med Mycol, /Cleveland//OH/44106; Case Western Reserve Univ, Dept Dermatol, /Cleveland//OH/44106; Univ Hosp Cleveland, Div Infect Dis, /Cleveland//OH/44106; Univ Illinois, Dept Vet Pathobiol, /Urbana//IL/61802
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF BACTERIOLOGY, 2001, V183, N18 (SEP), P5385-5394
GENUINE ARTICLE#: 467WT
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0021-9193
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Biofilms are a protected niche for microorganisms, where they are safe from antibiotic treatment and can create a source of persistent infection. Using two clinically relevant *Candida"** *albicans"** biofilm models formed on bioprosthetic materials, we demonstrated that biofilm formation proceeds through three distinct developmental phases. These growth phases transform adherent blastospores to well-defined cellular communities encased in a polysaccharide matrix. Fluorescence and confocal

scanning laser microscopy revealed that C. *albicans"** biofilms have a highly heterogeneous architecture composed of cellular and noncellular elements. In both models, antifungal resistance of biofilm-grown cells increased in conjunction with biofilm formation. The expression of *agglutinin"**-*like"** (*ALS"**) genes, which encode a family of proteins implicated in adhesion to host surfaces, was differentially regulated between planktonic and biofilm-grown cells. The ability of C. *albicans"** to form biofilms contrasts sharply with that of Saccharomyces cerevisiae, which adhered to bioprosthetic surfaces but failed to form a mature biofilm. The studies described here form the basis for investigations into the molecular mechanisms of *Candida"** biofilm biology and antifungal resistance and provide the means to design novel therapies for biofilm-based infections.

3/3,AB/12 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12638954 References: 52
TITLE: Characterization of *agglutinin"**-*like"** sequence genes from non-*albicans"** *Candida"** and phylogenetic analysis of the ALS family
AUTHOR(S): Hoyer LL (REPRINT); Fundyga R; Hecht JE; Kapteyn JC; Klis FM; Arnold J
AUTHOR(S) E-MAIL: lhoyer@uiuc.edu
CORPORATE SOURCE: 2522 VMBSB,2001 S Lincoln Ave, /Urbana//IL/61802 (REPRINT); Univ Illinois, Dept Vet Pathobiol, /Urbana//IL/61802; Univ Georgia, Dept Genet, /Athens//GA/30602; Univ Amsterdam, Swammerdam Inst Life Sci, /NL-1098 SM Amsterdam//Netherlands/
PUBLICATION TYPE: JOURNAL
PUBLICATION: GENETICS, 2001, V157, N4 (APR), P1555-1567
GENUINE ARTICLE#: 424GD
PUBLISHER: GENETICS, 428 EAST PRESTON ST, BALTIMORE, MD 21202 USA
ISSN: 0016-6731
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The *ALS"** (*agglutinin"**-*like"** sequence) gene family of *Candida"** *albicans"** encodes cell-surface glycoproteins implicated in adhesion of the organism to host surfaces. Southern blot analysis with ALS-specific probes suggested the presence of ALS gene families in C. dubliniensis and C. *tropicalis"**; three partial ALS genes were isolated from each organism. Northern blot analysis demonstrated that mechanisms governing expression of ALS genes in C. *albicans"** and C. dublininsis are different. Western blots with an anti-Als serum showed that cross-reactive proteins are linked by beta1,6-glucan in the cell wall of each non-*albicans"** *Candida"**, suggesting similar cell wall architecture and conserved processing of Als proteins in these organisms. Although and ALS family is present in each organism, phylogenetic analysis of the C. *albicans"**. C. dubliniensis, and C. *tropicalis"** ALS genes indicated that, within each species, sequence diversification in extensive and unique ALS sequences have arisen. Phylogenetic analysis of the ALS and SAP (secreted aspartyl proteinase) families show that the ALS family is younger than the SAP family. ALS genes in C. *albicans"**, C. dubliniensis, and C. *tropicalis"** tend to be located on chromosomes that also encode genes from the SAP family, yet the two families have unexpectedly different evolutionary histories. Homologous recombination between the tandem repeat sequences present in ALS genes could explain the different histories for co-localized genes in a predominantly clonal organism like C. ablicans.

3/3,AB/13 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12372391 References: 48
TITLE: The ALS5 gene of *Candida"** *albicans"** and analysis of the Als5p N-terminal domain
AUTHOR(S): Hoyer LL (REPRINT); Hecht JE
AUTHOR(S) E-MAIL: lhoyer@uiuc.edu
CORPORATE SOURCE: Univ Illinois, Dept Vet Pathobiol, 2522 VMBSB,2001 S Lincoln Ave/Urbana//IL/61802 (REPRINT); Univ Illinois, Dept Vet Pathobiol, /Urbana//IL/61802
PUBLICATION TYPE: JOURNAL
PUBLICATION: YEAST, 2001, V18, N1 (JAN 15), P49-60
GENUINE ARTICLE#: 394HK
PUBLISHER: JOHN WILEY & SONS LTD, BAFFINS LANE CHICHESTER, W SUSSEX PO19 1UD, ENGLAND
ISSN: 0749-503X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: ALS genes of *Candida"** *albicans"** encode a family of cell-surface glycoproteins with a three-domain structure. Each Als protein has a relatively conserved N-terminal domain, a central domain consisting of a tandemly repeated motif, and a serine-threonine-rich C-terminal domain that is relatively variable across the family, The ALS family exhibits several types of variability that indicate the importance of considering strain and allelic differences when studying ALS genes and their encoded proteins. Analysis of ALS5 provided additional evidence of variability within the ALS family. Comparison of the ALS5 sequence from two strains indicated sequence differences larger than strain or allelic mismatches observed for other C, *albicans"** genes. Screening a collection of commonly used C, *albicans"** strains and clinical isolates indicated that ALS5 is not present in several of these strains, supporting the conclusion that the Als protein profile is variable among C, *albicans"** isolates, Physical mapping of,ALS5 shelved that it is located close to *ALS1"** on chromosome 6, The N-terminal domain of ALs5p vc;as produced in Pichia pastoris to initiate structural analysis of this portion of the protein. The hydrophobic character of this portion of the protein was exploited in the purification scheme. Circular dichroism analysis of the purified, authenticated protein yielded a high content of antiparallel beta -sheet and Little to no alpha -helical structure. These results are consistent with the conclusion that the N-terminal domain of Als5p has an immunoglobulin fold structure similar to that found in many cell adhesion molecules. Gene sequences of C, *albicans"** ALS5 (Accession No. AF068866) and TPI1 (Accession No. AF124845) have been deposited in the GenBank database. Copyright (C) 2000 John Wiley & Sons, Ltd.

3/3,AB/14 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

11604929 References: 55
TITLE: TUP1, CPH1 and EFG1 make independent contributions to filamentation in *Candida"** *albicans"**
AUTHOR(S): Braun BR; Johnson AD (REPRINT)

AUTHOR(S) E-MAIL: ajohnson@socrates.ucsf.edu
CORPORATE SOURCE: Univ Calif San Francisco, Dept Microbiol, S-410,513 Parnassus Ave/San Francisco//CA/94143 (REPRINT); Univ Calif San Francisco, Dept Microbiol, /San Francisco//CA/94143
PUBLICATION TYPE: JOURNAL
PUBLICATION: GENETICS, 2000, V155, N1 (MAY), P57-67
GENUINE ARTICLE#: 311DH
PUBLISHER: GENETICS, 428 EAST PRESTON ST, BALTIMORE, MD 21202 USA
ISSN: 0016-6731
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The common fungal pathogen, *Candida"** *albicans"**, can grow either as single cells or as filaments (hyphae), depending on environmental conditions. Several transcriptional regulators have been identified as having key roles in controlling filamentous growth, including the products of the TUP1, CPH1, and EFG1 genes. We show, through a set of single, double, and triple mutants, that these genes act in an additive fashion to Control filamentous growth, suggesting that each gene represents a separate pathway of control. We also show that environmentally induced filamentous growth can occur even in the absence of all three of these genes, providing evidence for a fourth regulatory pathway. Expression of a collection of structural genes associated with filamentous growth, including HYR1, ECE1, HWP1, *ALS1"**, and CHS2, was monitored in strains lacking each combination of TUP1, EFG1, and CPH1. Different patterns of expression were observed among these target genes, supporting the hypothesis that these three regulatory proteins engage in a network of individual connections to downstream genes and arguing against a model whereby the target genes are regulated through a central filamentous growth pathway. The results suggest the existence of several distinct types of filamentous forms of C. *albicans"**, each dependent on a particular set of environmental conditions and each expressing a unique set of surface proteins.

3/3,AB/15 (Item 8 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

11365609 References: 52
TITLE: The cell wall architecture of *Candida"** *albicans"** wild-type cells and cell wall-defective mutants
AUTHOR(S): Kapteyn JC (REPRINT); Hoyer LL; Hecht JE; Muller WH; Andel A; Verkleij AJ; Makarow M; Van Den Ende H; Klis FM
AUTHOR(S) E-MAIL: kapteyn@bio.uva.nl
CORPORATE SOURCE: Univ Amsterdam, Swammerdam Inst Life Sci, Kruislaan 318/NL-1098 SM Amsterdam//Netherlands/ (REPRINT); Univ Amsterdam, Swammerdam Inst Life Sci, /NL-1098 SM Amsterdam//Netherlands/; Univ Illinois, Dept Vet Pathobiol, /Urbana//IL/61802; Univ Utrecht, Dept Mol Cell Biol, /NL-3584 CH Utrecht//Netherlands/; Univ Helsinki, Inst Biotechnol, /Helsinki//Finland/; Univ Kuopio, Dept Biochem & Biotechnol, /FIN-70211 Kuopio//Finland/
PUBLICATION TYPE: JOURNAL
PUBLICATION: MOLECULAR MICROBIOLOGY, 2000, V35, N3 (FEB), P601-611
GENUINE ARTICLE#: 285BF
PUBLISHER: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND
ISSN: 0950-382X
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: In *Candida"** *albicans"** wild-type cells, the beta

1,6-glucanase-extractable glycosylphosphatidylinositol (GPI)dependent cell wall proteins (CWPs) account for about 88% of all covalently linked CWPs. Approximately 90% of these GPI-CWPs, including *Als1p"** and Als3p, are attached via beta 1,6-glucan to beta 1,3-glucan. The remaining GPI-CWPs are linked through beta 1,6-glucan to chitin. The beta 1,6-glucanase-resistant protein fraction is small and consists of Pir-related CWPs, which are attached to beta 1,3-glucan through an alkalilabile linkage. Immunogold labelling and Western analysis, using an antiserum directed against Saccharomyces cerevisiae Pir2p/Hsp150, point to the localization of at least two differentially expressed Pir2 homologues in the cell wall of C. *albicans"**. In mnn9 Delta and pmt1 Delta mutant strains, which are defective in N- and O-glycosylation of proteins respectively, we observed enhanced chitin levels together with an increased coupling of GPI-CWPs through beta 1,6-glucan to chitin. In these cells, the level of Pir-CWPs was slightly upregulated. A slightly increased incorporation of Pir proteins was also observed in a beta 1,6-glucan-deficient hemizygous kre6 Delta mutant. Taken together, these observations show that C. *albicans"** follows the same basic rules as S. cerevisiae in constructing a cell wall and indicate that a cell wall salvage mechanism is activated when *Candida"** cells are confronted with cell wall weakening.

3/3,AB/16 (Item 9 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09909577 References: 56
TITLE: Identification of *Candida"** *albicans"** ALS2 and ALS4 and localization of ALS proteins to the fungal cell surface
AUTHOR(S): Hoyer LL (REPRINT); Payne TL; Hecht JE
CORPORATE SOURCE: UNIV ILLINOIS,DEPT VET PATHOBIOL, 2522 VMBSB, 2001 LINCOLN AVE/URBANA//IL/61802 (REPRINT)
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF BACTERIOLOGY, 1998, V180, N20 (OCT), P5334-5343
GENUINE ARTICLE#: 127JD
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
ISSN: 0021-9193
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Additional genes in the growing ALS family of *Candida"** *albicans"** were isolated by PCR screening of a genomic fosmid library with primers designed from the consensus tandem-repeat sequence of *ALS1"** , This procedure yielded fosmids encoding ALS2 and ALS4. ALS2 and ALS4 conformed to the three-domain structure of ALS genes, which consists of a central domain of tandemly repeated copies of a 108-bp motif, an upstream domain of highly conserved sequences, and a domain of divergent sequences 3 ' of the tandem repeats. Alignment of five predicted Als protein sequences indicated conservation of N- and C-terminal hydrophobic regions which have the hallmarks of secretory signal sequences and glycosylphosphatidylinositol addition sites, respectively. Heterologous expression of an N-terminal fragment of *Als1p"** in Saccharomyces cerevisiae demonstrated function of the putative signal sequence with cleavage following Ala17, This signal sequence cleavage site was conserved in the four other Als proteins analyzed, suggesting identical processing of each protein. Primary-structure features of the five Als proteins suggested a cell-surface localization, which was confirmed by indirect immunofluorescence with an anti-Als antiserum. Staining was observed on

mother yeasts and germ tubes, although the intensity of staining on the mother yeast decreased with elongation of the germ tube. Similar to other ALS genes, ALS2 and ALS4 were differentially regulated. ALS4 expression was correlated with the growth phase of the culture; ALS2 expression was not observed under many different in vitro growth conditions. The data presented here demonstrate that ALS genes encode cell-surface proteins and support the conclusion that the size and number of Als proteins on the C. *albicans"** cell surface vary,vith strain and growth conditions.

3/3,AB/17 (Item 10 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09757744 References: 56
TITLE: Multiple functions of Pmt1p-mediated protein O-mannosylation in the fungal pathogen *Candida"** *albicans"**
AUTHOR(S): Timpel C; StrahlBolsinger S; Ziegelbauer K; Ernst JF (REPRINT)
CORPORATE SOURCE: UNIV DUSSELDORF,INST MIKROBIOL, UNIV STR 1-26-12/D-40225 DUSSELDORF//GERMANY/ (REPRINT); UNIV DUSSELDORF,INST MIKROBIOL/D-40225 DUSSELDORF//GERMANY/; UNIV DUSSELDORF,BIOL MED FORSCHUNGSZENTRUM/D-40225 DUSSELDORF//GERMANY/; UNIV REGENSBURG,LEHRSTUHL ZELLBIOL & PFLANZENPHYSIOL/D-93040 REGENSBURG//GERMANY/; BAYER AG,LEHRSTUHL ZELLBIOL & PFLANZENPHYSIOL/D-42117 WUPPERTAL//GERMANY/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF BIOLOGICAL CHEMISTRY, 1998, V273, N33 (AUG 14), P 20837-20846
GENUINE ARTICLE#: 110MZ
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814
ISSN: 0021-9258
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Protein mannosylation by Pmt proteins initiates O-glycosylation in fungi, We have identified the PMT1 gene and analyzed the function of Pmt1p in the fungal human pathogen *Candida"** *albicans"**. Mutants defective in PMT1 alleles lacked Pmt in vitro enzymatic activity, showed reduced growth rates, and tended to for-m cellular aggregates. In addition, multiple specific deficiencies not known in Saccharomyces cerevisiae (including defective hyphal morphogenesis; supersensitivity to the antifungal agents hygromycin B, G418, clotrimazole, and calcofluor white; and reduced adherence to Caco-2 epithelial cells) were observed in pmt1 mutants. PMT1 deficiency also led to faster electrophoretic mobility of the *Als1p"** cell wall protein and to elevated extracellular activities of chitinase. Homozygous pmt1 mutants were avirulent in a mouse model of systemic infection, while heterozygous PMT1/pmt1 strains showed reduced virulence. The results indicate that protein O-mannosylation by Pmt proteins occurs in different fungal species, where PMT1 deficiency can lead to defects in multiple cellular functions.

3/3,AB/18 (Item 11 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09674219 References: 39
TITLE: *Candida"** *albicans"** ALS3 and insights into the nature of the ALS gene family

AUTHOR(S): Hoyer LL (REPRINT); Payne TL; Bell M; Myers AM; Scherer S
CORPORATE SOURCE: UNIV ILLINOIS,DEPT VET PATHOBIOL, 2522 VMBSB, 2001 S LINCOLN AVE/URBANA//IL/61802 (REPRINT); IOWA STATE UNIV SCI & TECHNOL,DEPT BIOCHEM & BIOPHYS/AMES//IA/50011; UNIV CALIF BERKELEY,LAWRENCE BERKELEY LAB, HUMAN GENOME CTR/BERKELEY//CA/94720; UNIV MINNESOTA,DEPT MICROBIOL/MINNEAPOLIS//MN/55455
PUBLICATION TYPE: JOURNAL
PUBLICATION: CURRENT GENETICS, 1998, V33, N6 (JUN), P451-459
GENUINE ARTICLE#: 101RU
PUBLISHER: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010
ISSN: 0172-8083
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The *ALS1"** (*agglutinin"**-*like"** sequence) gene of *Candida"** *albicans"** encodes a protein similar to alpha-agglutinin, a cell-surface adhesion glycoprotein of Saccharomyces cerevisiae (Hoyer et al. 1995). A central domain of a tandemly repeated 108-bp sequence is found in the *ALS1"** coding region. This tandem-repeat motif hybridizes to multiple C. *albicans"** genomic DNA fragments, indicating the possibility of other *ALS1"**-like genes in C. *albicans"** (Hoyer et al. 1995). To determine if these fragments constitute a gene family, tandem-repeat-hybridizing genomic fragments were isolated from a fosmid library by PCR screening using primers based on the consensus tandem-repeat sequence of *ALS1"** (Hoyer et al. 1995). One group of fosmids, designated ALS3, encodes a gene with 81% identity to *ALS1"**. The sequences of *ALS1"** and ALS3 are most conserved in the tandem-repeat domain and in the region 5' of the tandem repeats, Northern-blot analysis using unique probes from the 3' end of each gene demonstrated that *ALS1"** expression varies, depending on which C. *albicans"** strain is examined, and that,ALS3 is hyphal-specific. Both genes are found in a variety of C. *albicans"** and C. stellatoidea strains examined. The predicted *Als1p"** and Als3p exhibit features suggesting that both are cell-surface glycoproteins. Southern blots probed with conserved sequences from the region 5' of the tandem repeats suggest that other ALS-like sequences are present in the C. *albicans"** genome and that the ALS family may be larger than originally estimated.

3/3,AB/19 (Item 12 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09327986 References: 13
TITLE: Expression of the *Candida"** *albicans"** gene *ALS1"** in Saccharomyces cerevisiae induces adherence to endothelial and epithelial cells
AUTHOR(S): Fu Y; Rieg G; Fonzi WA; Belanger PH; Edwards JE; Filler SG (REPRINT)
CORPORATE SOURCE: UNIV CALIF LOS ANGELES,HARBOR RES & EDUC INST, ST, DIV INFECT DIS, DEPT MED/TORRANCE//CA/90502 (REPRINT); UNIV CALIF LOS ANGELES,HARBOR RES & EDUC INST, ST, DIV INFECT DIS, DEPT MED/TORRANCE//CA/90502; GEORGETOWN UNIV,DEPT MICROBIOL & IMMUNOL/WASHINGTON//DC/20007; UNIV CALIF LOS ANGELES,SCH MED/LOS ANGELES//CA/90024
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 1998, V66, N4 (APR), P1783-1786
GENUINE ARTICLE#: ZD630
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW,

WASHINGTON, DC 20005-4171
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: To identify genes encoding adhesins that mediate the binding of *Candida"** *albicans"** to endothelial cells, a genomic library from this organism was constructed and used to transform Saccharomyces cerevisiae. These transformed organisms were screened for adherence to endothelial cells, and a highly adherent clone was identified. The adherence of this clone to endothelial cells was over 100-fold greater than that of control S. cerevisiae transformed with the empty plasmid. This clone also exhibited enhanced adherence to epithelial cells. The C. *albicans"** gene contained within this clone was found to be *ALS1"**. These results indicate that *ALS1"** may encode a candidal adhesin.

3/3,AB/20 (Item 13 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06044548 References: 54
TITLE: *CANDIDA"** *ALBICANS"** *ALS1"** - DOMAINS RELATED TO A SACCHAROMYCES CEREVISIAE SEXUAL AGGLUTININ SEPARATED BY A REPEATING MOTIF
AUTHOR(S): HOYER LL; SCHERER S; SHATZMAN AR; LIVI GP
CORPORATE SOURCE: IOWA STATE UNIV SCI & TECHNOL,DEPT BIOCHEM & BIOPHYS/AMES//IA/50011 (Reprint); UNIV CALIF BERKELEY,LAWRENCE BERKELEY LAB,CTR HUMAN GENOME/BERKELEY//CA/94720; SMITHKLINE BEECHAM PHARMACEUT,DEPT GENE EXPRESSSCI/KING OF PRUSSIA//PA/19406
PUBLICATION: MOLECULAR MICROBIOLOGY, 1995, V15, N1 (JAN), P39-54
GENUINE ARTICLE#: PZ351
ISSN: 0950-382X
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Transfer of budding *Candida"** *albicans"** yeast cells from the rich, complex medium YEPD to the defined tissue culture medium RPMI 1640 (RPMI) at 37 degrees C and 5% CO2 causes rapid onset of hyphal induction. Among the genes induced under these conditions are hyphal-specific genes as well as genes expressed in response to changes in temperature, CO2 and specific media components. A cDNA library constructed from cells incubated for 20 min in RPMI was differentially screened with yeast (YEPD)- and hyphal (RPMI)-specific probes resulting in identification of a gene expressed in response to culture conditions but not regulated by the yeast-hyphal transition. The deduced gene product displays significant identity to Saccharomyces cerevisiae a-agglutinin, encoded by AG alpha 1, an adhesion glycoprotein that mediates mating of haploid cells. The presence of this gene in C. *albicans"** is curious since the organism has not. been observed to undergo meiosis. We designate the C. *albicans"** gene *ALS1"** (for *agglutinin"**-*like"** sequence). While the N- and C-termini of the predicted 1260-amino-acid *ALS1"** protein resemble those of the 650-amino-acid AG alpha 1, *ALS1"** contains a central domain of tandem repeats consisting of a highly conserved 36-amino-acid sequence not present in AG alpha 1. These repeats are also present on the nucleotide level as a highly conserved 108 bp motif. Southern and Northern blot analyses indicate a family of C. *albicans"** genes that contain the tandem repeat motif; at least one gene in addition to *ALS1"** is expressed under conditions similar to those for *ALS1"** expression. Genomic Southern blots from several C. *albicans"** isolates indicate that the number of copies of

the tandem repeat element in *ALS1"** differs across strains and, in some cases, between *ALS1"** alleles in the same strain, suggesting a strain-dependent variability in *ALS1"** protein size. Potential roles for the *ALS1"** protein are discussed.

3/3,AB/21 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01086530
Process for detecting primary signals of cell communication between cells of theimmune system
Verfahren zum Erfassen von Primarsignalen bei der Zellkommunikation von Zellen des Immunsystems
Procede de detection de signaux primaires de communication cellulaire entre cellules du systeme immunitaire
PATENT ASSIGNEE:
Holzel Diagnostika Handels GmbH, (2504010), Gereonswall 136, 50670 Koln, (DE), (Applicant designated States: all)
INVENTOR:
Holzel, Veit, Namibiastrasse 24, 50733 Koln, (DE)
LEGAL REPRESENTATIVE:
Patentanwalte Sternagel & Fleischer (101441), Braunsberger Feld 29, 51429 Bergisch Gladbach, (DE)
PATENT (CC, No, Kind, Date): EP 955544 A1 991110 (Basic)
APPLICATION (CC, No, Date): EP 98108220 980506;
DESIGNATED STATES: DE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: G01N-033/53
ABSTRACT EP 955544 A1 (Translated)
Detection of primary signals in immune cell communication useful for monitoring effects on immune system
A process for detecting primary cell signals in human or mammal cell communication in vitro, comprises:
(a) incubating the cells with polymer beads with diameter 5-100 mu m, which have been coated with at least one antibody, which is specific for these primary signals, under physiological conditions;
(b) exposing the cells to a stimulating factor, which causes the cells to release their primary signals, which then bind to the specific antibodies; and
(c) detecting the bound primary signals using labelled antibodies.
TRANSLATED ABSTRACT WORD COUNT: 96

ABSTRACT EP 955544 A1
Die Erfindung betrifft ein Verfahren zum Erfassen von Primarsignalen der Zellkommunikation von menschlichen und Saugetierzellen auserhalb eines Organismus, wobei Polymerkugelchen mit einem Durchmesser von 5 bis 100 (mu)m. die mindestens mit einem fur diese Primarsignale spezifischen Antikorper beladen sind, mit menschlichen oder Saugetierzellen, die Primarsignale aussenden konnen, gemischt und in Zellkultur unter physiologischen Bedingungen inkubiert werden, worin die Zellen durch einen externen Reiz zur Abgabe des Primarsignals stimuliert werden und die Polymerkugelchen die abgegebenen Primarsignale auffangen, welche anschliesend mit Hilfe eines weiteren Antikorpers, an den ein die Detektion zulassendes Molekul gekoppelt ist, mesbar gemacht werden.
ABSTRACT WORD COUNT: 96

LANGUAGE (Publication,Procedural,Application): German; German; German
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(German)	9945	372
SPEC A	(German)	9945	5599
Total word count - document A			5971
Total word count - document B			0
Total word count - documents A + B			5971

3/3,AB/22 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00623907
Immunoassay
Immunologischer Test
Essai immunologique
PATENT ASSIGNEE:
SEROSEARCH GmbH - ENTWICKLUNG UND KONZEPTION LABORDIAGNOSTISCHE PRODUKTE BERGHAUSEN, (1740760), Martin-Luther-Strasse 5, D-76327 Pfinztal, (DE), (applicant designated states: DE;FR;IT)
INVENTOR:
Naser, Karin, Dipl.-Biol., Lindpaintnerstrasse 85, D-70195 Stuttgart, (DE)
PATENT (CC, No, Kind, Date): EP 608791 A2 940803 (Basic)
EP 608791 A3 950712
EP 608791 B1 970709
APPLICATION (CC, No, Date): EP 94100924 940122;
PRIORITY (CC, No, Date): DE 4302012 930126
DESIGNATED STATES: DE; FR; IT
INTERNATIONAL PATENT CLASS: G01N-033/543; G01N-033/547; G01N-033/551; G01N-033/554;

ABSTRACT EP 608791 A2 (Translated)
The present invention relates to a method for the diagnostic determination of immunologically active material based on an agglutination reaction, its use and the articles needed therefor.
TRANSLATED ABSTRACT WORD COUNT: 29

ABSTRACT EP 608791 A2
Die vorliegende Erfindung betrifft ein Verfahren zur diagnostischen Bestimmung von immunologisch aktiven Material auf Basis einer Agglutinationsreaktion, deren Anwendung und die dafur benotigten Gegenstande.
ABSTRACT WORD COUNT: 26

LANGUAGE (Publication,Procedural,Application): German; German; German
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(German)	EPABF2	811
CLAIMS B	(English)	EPAB97	937
CLAIMS B	(German)	EPAB97	841
CLAIMS B	(French)	EPAB97	1028
SPEC A	(German)	EPABF2	6957
SPEC B	(German)	EPAB97	6874
Total word count - document A			7770
Total word count - document B			9680

Total word count - documents A + B 17450

3/3,AB/23 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00465029
Filamentous hemagglutinin of bordetella pertussis as a carrier molecule for conjugate vaccines.
Faser-*Hemagglutinin"** von Bordetella pertussis *als"** Trager fur konjugierten Impfstoff.
Hemagglutinine filamenteuse de Bordetella pertussis a titre de molecules porteuses pour vaccins conjugues.
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212594), One Cyanamid Plaza, Wayne, NJ 07470-8426, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;NL;SE)
INVENTOR:
Kimura, Alan, 9856 N.W. 52 Terrace, Miami, FL 33178, (US)
Dick, William Edwin JR., 754 Hawthorne Place, Webster, NY, (US)
Cowell, James Leo, 37 Sugarmills Circle, Fairport, NY 14450, (US)
LEGAL REPRESENTATIVE:
Wachtershauser, Gunter, Prof. Dr. (12711), Patentanwalt, Tal 29, D-80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 471177 A2 920219 (Basic)
EP 471177 A3 930224
EP 471177 B1 951004
APPLICATION (CC, No, Date): EP 91110919 910702;
PRIORITY (CC, No, Date): US 565161 900813
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/10; A61K-039/385;

ABSTRACT EP 471177 A2
This invention pertains to immunogenic conjugates comprising an antigen bound to a filamentous hemagglutinin of Bordetella pertussis and a method of eliciting an immune response against an antigen comprising administering such an immunogenic conjugate with a pharmaceutically acceptable vehicle to a vertebrate host.
ABSTRACT WORD COUNT: 45

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	232
CLAIMS B	(English)	EPAB95	232
CLAIMS B	(German)	EPAB95	248
CLAIMS B	(French)	EPAB95	257
SPEC A	(English)	EPABF1	2515
SPEC B	(English)	EPAB95	2436
Total word count - document A			2747
Total word count - document B			3173
Total word count - documents A + B			5920

3/3,AB/24 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00301729
Medicament containing a polysaccharidic component from thuja plants as the active ingredient.
Arzneimittel mit einem Gehalt an einer Polysaccharide enthaltenden Komponente aus Thujapflanzen als aktivem Wirkstoff.
Medicament contenant comme agent actif un composant polysaccharidique de plantes de thuja.
PATENT ASSIGNEE:
Neth, Rolf Dietmar, Prof. Dr., (1033840), Pennskuhle 9, W-2110 Buchholz, (DE), (applicant designated states:
AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
STIFTUNG ZUR FORDERUNG DER ERFAHRUNGSHEILKUNDE IM STIFTERVERBAND FUR DIE DEUTSCHE WISSENSCHAFT, (1033850), Brucker Holt 56-60, W-4300 Essen 1, (DE), (applicant designated states:
AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Gohla, Sven, Waitzstrasse 17, W-2000 Hamburg 52, (DE)
Neth, Rolf Dietmar, Prof. Dr., Pennskuhle 9, W-2110 Buchholz, (DE)
Haubeck, Hans-Dieter, Dr., Veghestrasse 10, W-4400 Munster/Westf., (DE)
LEGAL REPRESENTATIVE:
UEXKULL & STOLBERG Patentanwalte (100011), Beselerstrasse 4, W-2000 Hamburg 52, (DE)
PATENT (CC, No, Kind, Date): EP 315182 A2 890510 (Basic)
EP 315182 A3 890628
EP 315182 B1 911127
APPLICATION (CC, No, Date): EP 88118394 881104;
PRIORITY (CC, No, Date): DE 3738319 871106; DE 3822945 880707
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-031/715; A61K-035/78;

ABSTRACT EP 315182 A2 (Translated)
The plant component achieves a specific induction of the lymphocytic T-helper cell fraction of the peripheral blood. The specific induction of the fraction of T-helper cells is associated with the expression of the T-helper cell activation markers OKT 17 and OKT 26a and with an increased interleukin-2 synthesis.
The component furthermore stimulates leukocyte formation and has a protective effect against stress due to radioactive emissions.
TRANSLATED ABSTRACT WORD COUNT: 67

ABSTRACT EP 315182 A2
Es werden Arzneimittel mit einer aus Thujapflanzen gewonnenen Polysaccharide enthaltende Komponente als aktivem Wirkstoff beschrieben.
Mit der pflanzlichen Komponente wird eine spezifische Induktion der lymphozytaren T-Helferzellfraktion des peripheren Blutes erzielt. Die spezifische Induktion der Fraktion der T-Helferzellen ist verbunden mit der Expression der T-Helferzellaktivierungsmarker Okt 17 und Okt 26a sowie einer erhohten Interleukin-2 Synthese.
Die erfindungsgemase Komponente stimuliert ferner die Leukozytenbildung und ubt eine protektive Wirkung ggenuber Belastungen durch radioaktive Strahlen aus.
ABSTRACT WORD COUNT: 76

LANGUAGE (Publication,Procedural,Application): German; German; German
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	443

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      CLAIMS B    (German)  EPBBF1      375
      CLAIMS B    (French)  EPBBF1      468
      SPEC B      (German)  EPBBF1     4001
Total word count - document A             0
Total word count - document B          5287
Total word count - documents A + B     5287

Set     Items   Description
S4       7686   AU=(EDWARDS, J? OR EDWARDS J?)
S5        178   AU=(FILER S? OR FILER, S? OR FILLER, S? OR FILLER S?)
S6        741   AU=(CUTLER, J? OR CUTLER J?)
S7        726   AU=(SHEPPARD, D? OR SHEPPARD D?)
S8       1941   AU=(IBRAHIM, A? OR IBRAHIM A?)
S9       3493   AU=(FU, Y? OR FU Y?)
S10         2   S4 AND S5 AND S6 AND S7 AND S8 AND S9
S11       112   S4 AND (S5 OR S6 OR S7 OR S8 OR S9)
S12        36   S5 AND (S6 OR S7 OR S8 OR S9)
S13         4   S6 AND (S7 OR S8 OR S9)
S14         3   S7 AND (S8 OR S9)
S15        19   S8 AND S9
S16        13   (S5 OR S6 OR S7 OR S8 OR S9 OR S11 OR S4) AND S1
S17        47   (S10 OR S12 OR S13 OR S14 OR S15 OR S16) NOT S2
S18        16   RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113
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- Author(s)

18/3,AB/1 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

14170743 PASCAL No.: 99-0369085

Unanticipated heterogeneity in growth rate and virulence among Candida albicans AAF1 null mutants

RIEG G; YUE FU; *IBRAHIM A S"**; XIANG ZHOU; *FILLER S G"**; EDWARDS J E JR

Division of Infectious Diseases, St. John's Cardiovascular Research Center, Department of Medicine, Harbor-UCLA Research and Education Institute, Torrance, California 90502, United States; UCLA School of Medicine, Los Angeles, California 90024, United States

Journal: Infection and immunity, 1999, 67 (7) 3193-3198

Language: English

The disruption of a specific gene in Candida albicans is commonly used to determine the function of the gene product. We disrupted AAF1, a gene of C. albicans that causes Saccharomyces cerevisiae to flocculate and adhere to endothelial cells. We then characterized multiple heterozygous and homozygous mutants. These null mutants adhered to endothelial cells to the same extent as did the parent organism. However, mutants with presumably the same genotype revealed significant heterogeneity in their growth rates in vitro. This heterogeneity was not the result of the transformation procedure per se, nor was it caused by differences in the expression or function of URA3, a marker used in the process of gene disruption. The growth rate among the different heterozygous and homozygous null mutants was positively correlated with in vivo virulence in mice. It is possible that the variable phenotypes of C. albicans were due to mutations outside of the AAF1 coding region that were introduced during the gene disruption process. These results indicate that careful phenotypic characterization of mutants of C. albicans generated through targeted gene disruption should be performed to exclude the introduction of unexpected mutations that may influence pathogenicity in mice.

18/3,AB/2 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

13827102 PASCAL No.: 99-0002581
Mechanism of fluconazole resistance in Candida krusei
OROZCO A S; HIGGINBOTHAM L M; HITCHCOCK C A; PARKINSON T; FALCONER D; *IBRAHIM A S"**; GHANNOUM M A; *FILLER S G"**
St. John's Cardiovascular Research Center, Division of Infectious Diseases, Harbor-UCLA Research and Education Institute, Torrance, California 90502, United States; Pfizer Central Research, Sandwich, Kent, United Kingdom; UCLA School of Medicine, Los Angeles, California 90024, United States
Journal: Antimicrobial agents and chemotherapy, 1998, 42 (10) 2645-2649
Language: English
The mechanisms of fluconazole resistance in three clinical isolates of Candida krusei were investigated. Analysis of sterols of organisms grown in the absence and presence of fluconazole demonstrated that the predominant sterol of C. krusei is ergosterol and that fluconazole inhibits 14 alpha -demethylase in this organism. The 14 alpha -demethylase activity in cell extracts of C. krusei was 16- to 46-fold more resistant to inhibition by fluconazole than was 14 alpha -demethylase activity in cell extracts of two fluconazole-susceptible strains of Candida albicans. Comparing the carbon monoxide difference spectra of microsomes from C. krusei with those of microsomes from C. albicans indicated that the total cytochrome P-450 content of C. krusei is similar to that of C. albicans. The Soret absorption maximum in these spectra was located at 448 nm for C. krusei and at 450 nm for C. albicans. Finally, the fluconazole accumulation of two of the C. krusei isolates was similar to if not greater than that of C. albicans. Thus, there are significant qualitative differences between the 14 alpha -demethylase of C. albicans and C. krusei. In addition, fluconazole resistance in these strains of C. krusei appears to be mediated predominantly by a reduced susceptibility of 14 alpha -demethylase to inhibition by this drug.

18/3,AB/3 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

13660087 PASCAL No.: 98-0367399
Secreted aspartyl proteinases and interactions of Candida albicans with human endothelial cells
*IBRAHIM A S"**; *FILLER S G"**; SANGLARD D; EDWARDS J E JR; HUBE B
Division of Infectious Diseases, St. John's Cardiovascular Research Center, Department of Medicine, Harbor-UCLA Research and Education Institute, Torrance, California 90509, United States; UCLA School of Medicine, Los Angeles, California 90024, United States; Institut de Microbiologie, Centre Hospitalier Universitaire Vaudois, 1011 Lausanne, Switzerland; Institut fuer Allgemeine Botanik, AMP III, Universitaet Hamburg, 22609 Hamburg, Germany
Journal: Infection and immunity, 1998, 66 (6) 3003-3005

Language: English

The endothelial cell interactions of homozygous null mutants of Candida albicans that were deficient in secreted aspartyl proteinase 1 (Sap1), Sap2, or Sap3 were investigated. Only Sap2 was found to contribute to the ability of C. albicans to damage endothelial cells and stimulate them to express E-selectin. None of the Saps studied appears to play a role in C. albicans adherence to endothelial cells.

18/3,AB/4 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal

13587939 PASCAL No.: 98-0291844

Cloning and characterization of CAD1/AAF1, a gene from Candida albicans that induces adherence to endothelial cells after expression in Saccharomyces cerevisiae

YUE FU; *FILLER S G"**; SPELLBERG B J; FONZI W; *IBRAHIM A S"**; KANBE T; GHANNOUM M A; EDWARDS J E JR

St. John Cardiovascular Research Center, Division of Infectious Diseases, Department of Medicine, Harbor-UCLA Research and Education Institute, Torrance California 90502, United States; Department of Microbiology and Immunology, Georgetown University, Washington, DC 20007, United States; School of Medicine, University of California Los Angeles, Los Angeles, California 90024, United States; Laboratory of Medical Mycology, Research Institute for Disease Mechanisms and Control, Nagoya University School of Medicine, Nagoya 466, Japan

Journal: Infection and immunity, 1998, 66 (5) 2078-2084

Language: English

Adherence to the endothelial cell lining of the vasculature is probably a critical step in the egress of Candida albicans from the intravascular compartment. To identify potential adhesins that mediate the attachment of this organism to endothelial cells, a genomic library from C. albicans was used to transform a nonadherent strain of Saccharomyces cerevisiae. The population of transformed yeasts was enriched for highly adherent clones by repeated passages over endothelial cells. One clone which exhibited a fivefold increase in endothelial cell adherence, compared with S. cerevisiae transformed with vector alone, was identified. This organism also flocculated. The candidal DNA fragment within this adherent/flocculent organism was found to contain a single 1.8-kb open reading frame, which was designated CADI. It was found to be identical to AAFI. The predicted protein encoded by CADI/AAF1 contained features suggestive of a regulatory factor. Consistent with this finding, immunoelectron microscopy revealed that CAD1/AAF1 localized to the cytoplasm and nucleus but not the cell wall or plasma membrane of the transformed yeasts. Because yeasts transformed with CAD1/AAF1 both flocculated and exhibited increased endothelial cell adherence, the relationship between adherence and flocculation was examined. S. cerevisiae expressing either of two flocculation phenotypes, Flo1 or NewFlo, adhered to endothelial cells as avidly as did yeasts expressing CAD1/AAFI. Inhibition studies revealed that the flocculation phenotype induced by CAD1/AAF1 was similar to Flo1. Thus, CAD1/AAF1 probably encodes a regulatory protein that stimulates endothelial cell adherence in S. cerevisiae by inducing a flocculation phenotype. Whether CAD1/AAF1 contributes to the adherence of C. albicans to endothelial cells remains to be determined.

18/3,AB/5 (Item 5 from file: 144)
DIALOG(R)File 144:Pascal

12898617 PASCAL No.: 97-0164050
Cloning and characterization of a gene (LIP1) which encodes a lipase from the pathogenic yeast Candida albicans : Candida albicans
*FU Y"**; *IBRAHIM A S"**; FONZI W; ZHOU X; RAMOS C F; GHANNOUM M A
Division of Infectious Diseases, St John's Cardiovascular Research Center, Department of Medicine, Harbour-UCLA Medical Center, Torrance, CA 90509, United States; Department of Microbiology and Immunology, School of Medicine, Georgetown University Medical Center, Washington, DC 20007-2197, United States; University Center for Medical Mycology, Department of Dermatology, Case Western Reserve University and University Hospitals of Cleveland, 11100 Euclid Avenue, Stop LKS 5028, Cleveland, OH 44106-5028, United States; Mycology Reference Laboratory, Department of Dermatology, Case Western Reserve University and University Hospitals of Cleveland, 11100 Euclid Avenue, Stop LKS 5028, Cleveland, OH 44106-5028, United States
Journal: Microbiology : (Reading), 1997, 143 (p.2) 331-340
Language: English
Extracellular phospholipases are demonstrated virulence factors for a number of pathogenic microbes. The opportunistic pathogen Candida albicans is known to secrete phospholipases and these have been correlated with strain virulence. In an attempt to clone C. albicans genes encoding secreted phospholipases, Saccharomyces cerevisiae was transformed with a C albicans genomic library and screened for lipolytic activity on egg-yolk agar plates, a traditional screen for phospholipase activity. Two identical clones were obtained which exhibited lipolytic activity. Nucleotide sequence analysis identified an ORF encoding a protein of 351 amino acid residues. Although no extensive homologies were identified, the sequence contained the Gly-X-Ser-X-Gly motif found in prokaryotic and eukaryotic lipases, suggesting a similar activity for the encoded protein. Indeed, culture supernatants from complemented yeast cells contained abundant hydrolytic activity against a triglyceride substrate and had no phospholipase activity. The data suggest that C. albicans, in addition to phospholipases, also has lipases. Southern blot analyses revealed that C. albicans may contain a lipase gene (LIP) family, and that a lipase gene(s) may be present in Candida parapsilosis, Candida tropicalis and Candida krusei, but not in Candida pseudotropicalis, Candida glabrata or S. cerevisiae. Northern blot analyses showed that expression of the LIP1 transcript, the cloned gene which encodes a lipase, was detected only when C. albicans was grown in media containing Tween 80, other Tweens or triglycerides as the sole carbon source, and not in Sabouraud Dextrose Broth or yeast/peptone/dextrose media. Additionally, carbohydrate supplementation inhibited LIP1 expression. Cloning this gene will allow the construction of LIP1deficient null mutants which will be critical in determining the role of this gene in candidal virulence.

18/3,AB/6 (Item 6 from file: 144)
DIALOG(R)File 144:Pascal

12361226 PASCAL No.: 96-0005868
Adherence to and damage of endothelial cells by Cryptococcus neoformans

in vitro : role of the capsule
*IBRAHIM A S"**; *FILLER S G"**; ALCOULOUMRE M S; KOZEL T R; EDWARDS J E JR; GHANNOUM M A
Harbor-UCLA, res. education inst., div. infectious diseases, Torrance CA 90509, USA
Journal: Infection and immunity, 1995, 63 (11) 4368-4374
Language: English
Escape from the intravascular compartment is likely a critical step in the development of hematogenously disseminated cryptococcal infections, such as meningitis. The capsule of Cryptococcus neoformans is considered to be a virulence factor because of its antiphagocytic properties. To further investigate the role of the capsule in escape from the intravascular compartment, we used isogenic strain pairs, an acapsular mutant, and an encapsulated clinical isolate to determine the effects of the capsule of C. neoformans on adherence to, phagocytosis by, and damage of endothelial cells in vitro. Acapsular C. neoformans adhered significantly more to endothelial cells and caused greater endothelial cell injury than did encapsulated organisms. Coating of an acapsular strain with cryptococcal glucuronoxylomannan decreased both adherence to and damage of endothelial cells by 61.7% +- 9.1% and 76.6% +- 10.2%, respectively. Transmission electron microscopy demonstrated internalization ofacapsular, but not encapsulated, organisms by endothelial cells. Internalization of an acapsular strain occurred through endothelial cell phagocytosis and was inhibited by cytochalasin D. Phagocytosis required a heat-labile serum factor, probably complement. These results suggest that acapsular or poorly encapsulated C. neoformans may be the form(s) that escapes from the vasculature during initiation of hematogenously disseminated disease.

18/3,AB/7 (Item 7 from file: 144)
DIALOG(R)File 144:Pascal

12112423 PASCAL No.: 95-0342677
Evidence implicating phospholipase as a virulence factor of Candida albicans
*IBRAHIM A S"**; MIRBOD F; *FILLER S G"**; BANNO Y; COLE G T; KITAJIMA Y; EDWARDS J E JR; NOZAWA Y; GHANNOUM M A
Harbor-UCLA, res. education inst., div. infectious diseases, Torrance CA 90502, USA
Journal: Infection and immunity, 1995, 63 (5) 1993-1998
Language: English
Three different approaches were used to investigate the role of extracellular phospholipases in the pathogenicity of Candida albicans. First, we compared 11 blood isolates of this yeast with an equal number of commensal strains isolated from the oral cavities of healthy volunteers. Blood isolates produced significantly more extracellular phospholipase activity than the commensal strains did. Second, two clinical isolates of C. albicans that differed in their levels of virulence in a newborn mouse model were compared for their ability to secrete phospholipases. The invasive strain produced significantly more extracellular phospholipase activity than the noninvasive strain did. Third, nine blood isolates were characterized for their phospholipase and proteinase production, germ tube formation, growtb, and adherence to and damage of endothelial cells in vitro. These factors were analyzed subsequently to determine whether they predicted mortality in a mouse model of hematogenously disseminated candidiasis. By proportional hazard analysis, the relative risk of death was 5.6-fold bigber (95% confidence interval, 1.672 to 18.84 (P<0.005)) in

the mice infected with the higher-phospholipase-secreting strains than in the low-phospholipase secretors. None of the other putative virulence factors predicted mortality. Characterization of phospholipases secreted by three of the blood isolates showed that these strains secreted bot phospholipase B and lysophospholipase-transacylase activities. These results implicate extracellular phospholipase as a virulence factor in the pathogenesis of hematogenous infections caused by C. albicans

18/3,AB/8 (Item 8 from file: 144)
DIALOG(R)File 144:Pascal

11474042 PASCAL No.: 94-0311301
Mechanisms by which Candida albicans induces endothelial cell prostaglandin synthesis
*FILLER S G"**; IBE B O; *IBRAHIM A S"**; GHANNOUM M A; USHA RAJ J; EDWARDS J E JR
UCLA, school medicine, div. infectious diseases, Torrance CA 90509, USA
Journal: Infection and immunity, 1994, 62 (3) 1064-1069
Language: English
One strategy for improving resistance to opportunistic pathogens is to determine host cellular responses during the invasion process and upregulate those responses that are relevant to host defense mechanisms. Within this context, we have shown previously that invasion of endothelial cells by Candida albicans in vitro causes increased production of prostaglandins. As a prerequisite for modulating endothelial cell prostaglandin production, we now characterize the mechanisms through which this process occurs. Endothelial cell invasion by C. albicans appeared to stimulate the conversion of arachidonic acid into prostaglandins by upregulating the synthesis of endothelial cell cyclooxygenase and increasing the activity of the endothelial cell phospholipase

18/3,AB/9 (Item 9 from file: 144)
DIALOG(R)File 144:Pascal

10988500 PASCAL No.: 93-0498005
Interferon- gamma protects endothelial cells from damage by Candida albicans
*IBRAHIM A S"**; *FILLER S G"**; GHANNOUM M A; EDWARDS J E JR
Harbor-UCLA medical cent., dep. internal medicine, div. infectious diseases, Torrance CA 90509, USA
Journal: The Journal of infectious diseases, 1993, 167 (6) 1467-1470
Language: English
Endothelial cells activated with interferon- gamma (IFN- gamma) have been shown to inhibit the replication of Toxoplasma gondii. To determine if this cytokine protects endothelial cells from damage by Candida albicans, human umbilical vein endothelial cells were pretreated with IFN- gamma and infected with C. albicans; endothelial cell damage was measured by the release of SUP 5 SUP 1 Cr. Pretreatment with IFN- gamma decreased the extent of endothelial cell injury caused by C. albicans by up to 100% +- 8.2%. This diminution of endothelial cell damage was confirmed by scanning electron microscopy. The degree of protection was dependent on the concentration of IFN- gamma , with maximum protection occurring at 13 units/mL

18/3,AB/10 (Item 10 from file: 144)
DIALOG(R)File 144:Pascal

10501149 PASCAL No.: 93-0010400
Modulation of interactions of Candida albicans and endothelial cells by fluconazole and amphotericin B
GHANNOUM M A; *FILLER S G"**; *IBRAHIM A S"**; YUE FU; EDWARDS J E JR
Harbor-univ. California, Los Angeles medical cent., div. adult infectious diseases, Torrance CA 90509, USA
Journal: Antimicrobial agents and chemotherapy, 1992, 36 (10) 2239-2244
Language: English
Using an in vitro model of intravascular infection, we examined the effects of exposure to subinhibitory concentrations of fluconazole and amphotericin B on the ability of Candida albicans to adhere to and damage human umbilical vein endothelial cells. Incubation of the organisms for 18 h in 0.5x the MICs of fluconazole and amphotericin B inhibited endothelial cell adherence by 22 and 91%, respectively (P<0.001 for each drug). Candida-induced endothelial cell injury was also decreased by exposing the organisms to the antifungal drugs while in contact with the endothelial cells

18/3,AB/11 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12427747 References: 82
TITLE: Pathogenesis I: interactions of host cells and fungi
AUTHOR(S): Clemons KV (REPRINT); Calich VLG; Burger E; *Filler SG"**; Graziutti M; Murphy J; Roilides E; Campa A; Dias MR; Edwards JE; *Fu Y"** ; Fernandes-Bordignon G; Ibrahim Z; Katsifa H; Lamaignere CG; Meloni-Bruneri LH; Rex J; Savary CA; Xidieh C
AUTHOR(S) E-MAIL: Karl.Clemons@slip.net
CORPORATE SOURCE: Santa Clara Valley Med Ctr, Div Infect Dis, 751 S Bascom Ave/San Jose//CA/95128 (REPRINT); Santa Clara Valley Med Ctr, Div Infect Dis, /San Jose//CA/95128; Calif Inst Med Res, /San Jose//CA/95128; Stanford Univ, Div Infect Dis & Geog Med, /Stanford//CA/94305; Univ Sao Paulo, Dept Imunol ICB, /Sao Paulo//Brazil/; Univ Sao Paulo, Dept Anal Clin & Toxicol FCF, /Sao Paulo//Brazil/; Harbor UCLA Res & Educ Inst, Dept Med, /Torrance//CA/; Univ Calif Los Angeles, Sch Med, /Los Angeles//CA/; Fdn Ctr Estudios Infect, /Buenos Aires/DF/Argentina/; Univ Texas, Dept Surg Oncol, /Houston//TX/77030; Univ Texas, Dept Mol & Cellular Oncol, /Houston//TX/77030; Univ Texas, Dept Internal Med, /Houston//TX/; Univ Oklahoma, Dept Microbiol & Immunol, /Oklahoma City//OK/73190; Univ Thessaloniki, Dept Pediat 3, /GR-54006 Salonika//Greece/
PUBLICATION TYPE: JOURNAL
PUBLICATION: MEDICAL MYCOLOGY, 2000, V38, ,1, P99-111
GENUINE ARTICLE#: 401ZE
PUBLISHER: B I O S SCIENTIFIC PUBLISHERS LTD, 9 NEWTEC PLACE, MAGDALEN RD, OXFORD OX4 1RE, ENGLAND
ISSN: 1369-3786
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The interactions of host cells and fungi during infection represent a complex interplay. Although T helper 1 (Th1)-mediated immunity

is primarily responsible for acquired resistance to Paracoccidioides brasiliensis, studies have demonstrated that polymorphonuclear neutrophils play a critical role in providing an early resistance to this organism. One study has shown that the invasiveness of Candida albicans requires adherence, particularly to endothelial cells, which in turn are stimulated to express various cell-markers and pro-inflammatory cytokines as part of a proactive resistance to invasion. Somewhat in contrast to infection with C. albicans, it has been shown that the capsular glucuronoxylomannan of Cryptococcus neoformans causes the shedding of host-cell adherence molecules (L-selectins) needed for the migration of host-inflammatory cells to sites of infection and likely explains, in part, the reduced host inflammatory response to this organism. Resistance to aspergillosis is often associated with the immune status of the host. In one set of studies, it has been demonstrated that lymphocytes have little direct effect on the organism, but that antigen-presenting dendritic cells stimulate the production of Th1 cytokines, suggesting a positive role for the dendritic cell in host-response. Similarly, another study has shown that among the regulatory cytokine networks that Th2-associated cytokines (e.g., interleukin-10) likely play a detrimental role in the resistance of the host to Aspergillus fumigatus.

18/3,AB/12 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09896968 References: 52
TITLE: Cloning and disruption of caPLB1, a phospholipase B gene involved in the pathogenicity of Candida albicans
AUTHOR(S): Leidich SD; *Ibrahim AS"**; *Fu Y"**; Koul A; Jessup C; Vitullo J; Fonzi W; Mirbod F; Nakashima S; Nozawa Y; Ghannoum MA (REPRINT)
CORPORATE SOURCE: UNIV HOSP CLEVELAND,CTR MED MYCOL, 11100 EUCLID AVE/CLEVELAND//OH/44106 (REPRINT); UNIV HOSP CLEVELAND,CTR MED MYCOL/CLEVELAND//OH/44106; CASE WESTERN RESERVE UNIV,/CLEVELAND//OH/44106 ; UNIV CALIF LOS ANGELES,HARBOR MED CTR, DEPT MED, DIV INFECT DIS, ST JOHNS CARDIOVASC RES CTR/TORRANCE//CA/90509; GEORGETOWN UNIV,MED CTR, SCH MED, DEPT MICROBIOL & IMMUNOL/WASHINGTON//DC/20007; GIFU UNIV,SCH MED, DEPT BIOCHEM/GIFU 500//JAPAN/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF BIOLOGICAL CHEMISTRY, 1998, V273, N40 (OCT 2), P 26078-26086
GENUINE ARTICLE#: 125XU
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814
ISSN: 0021-9258
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: The Candida albicans PLB1 gene was cloned using a polymerase chain reaction-based approach relying on degenerate oligonucleotide primers designed according to the amino acid sequences of two peptide fragments obtained from a purified candidal enzyme displaying phospholipase activity (Mirbod, F., Banno, Y., Ghannoum, M. A, Ibrahim, A. S., Nakashima, S., Yasuo, It., Cole, G. T., and Nozawa, Y. (1995) Biochim. Biophys. Acta 1257, 181-188). Sequence analysis of a 6.7-kilobase pair EcoRI-ClaI genomic clone revealed a single open reading frame of 1818 base pairs that predicts for a preprotein of 605 residues. Comparison of the putative candidal phospholipase with those of other proteins in data base revealed significant homology to known fungal phospholipase Bs from Saccharomyces cerevisiae (45%), Penicillium notatum (42%), Torulaspora delbrueckii (48%),

and Schizosaccharomyces pombe (38%). Thus, we have cloned the gene encoding a C. albicans phospholipase B homolog. This gene, designated caPLB1, was mapped to chromosome 6. Disruption experiments revealed that the caplb1 null mutant is viable and displays no obvious phenotype. However, the virulence of strains deleted for caPLB1, as assessed in a murine model for hematogenously disseminated candidiasis, was significantly attenuated compared with the isogenic mild-type parental strain. Although deletion of caPLB1 did not produce any detectable effects on candidal adherence to human endothelial or epithelial cells, the ability of the caplb1 null mutant to penetrate host cells was dramatically reduced. Thus, phospholipase B may well contribute to the pathogenicity of C. albicans by abetting the fungus in damaging and traversing host cell membranes, processes which likely increase the rapidity of disseminated infection.

18/3,AB/13 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09439010 References: 32
TITLE: Cloning and characterization of CAD1/AAF1, a gene from Candida albicans that induces adherence to endothelial cells after expression in Saccharomyces cerevisiae
AUTHOR(S): *Fu Y"**; *Filler SG"**; Spellberg BJ; Fonzi W; *Ibrahim AS"**; Kanbe T; Ghannoum MA; Edwards JE (REPRINT)
CORPORATE SOURCE: UNIV CALIF LOS ANGELES,LOS ANGELES CTY HARBOR MED CTR, ST JOHNS CARDIOVASC RES CTR, DEPT MED/TORRANCE//CA/90502 (REPRINT); UNIV CALIF LOS ANGELES,LOS ANGELES CTY HARBOR MED CTR, ST JOHNS CARDIOVASC RES CTR, DEPT MED/TORRANCE//CA/90502; UNIV CALIF LOS ANGELES,SCH MED/LOS ANGELES//CA/90024; GEORGETOWN UNIV,DEPT MICROBIOL & IMMUNOL/WASHINGTON//DC/20007; NAGOYA UNIV,SCH MED, DIS MECHANISM & CONTROL RES INST, MED MYCOL LAB/NAGOYA/AICHI 466/JAPAN/
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 1998, V66, N5 (MAY), P2078-2084
GENUINE ARTICLE#: ZL243
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: Adherence to the endothelial cell lining of the vasculature is probably a critical step in the egress of Candida albicans from the intravascular compartment. To identify potential adhesins that mediate the attachment of this organism to endothelial cells, a genomic library from C. albicans was used to transform a nonadherent strain of Saccharomyces cerevisiae. The population of transformed yeasts was enriched for highly adherent clones by repeated passages over endothelial cells, One clone which exhibited a fivefold increase in endothelial cell adherence, compared with S. cerevisiae transformed with vector alone, was identified, This organism also flocculated. The candidal DNA fragment within this adherent/flocculent organism was found to contain a single 1,8-kb open reading frame, which was designated CAD1. It was found to be identical to AAF1. The predicted protein encoded by CAD1/AAF1 contained features suggestive of a regulatory factor. Consistent with this finding, immunoelectron microscopy revealed that CAD1/AAF1 localized to the cytoplasm and nucleus but not the cell wall or plasma membrane of the transformed yeasts. Because yeasts transformed with CAD1/AAF1 both flocculated and exhibited increased endothelial cell adherence, the relationship between adherence and flocculation mas examined. S. cerevisiae

expressing either of two flocculation phenotypes, Flo1 or NewFlo, adhered to endothelial cells as avidly as did yeasts expressing CAD1/AAF1. Inhibition studies revealed that the flocculation phenotype induced by CAD1/AAF1 was similar to Flo1. Thus, CAD1/AAF1 probably Encodes a regulatory protein that stimulates endothelial cell adherence in S. cerevisiae by inducing a flocculation phenotype. Whether CAD1/AAF1 contributes to the adherence of C. albicans to endothelial cells remains to be determined.

18/3,AB/14 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08184856 References: 39
TITLE: Cloning and characterization of a gene (LIP1) which encodes a lipase from the pathogenic yeast Candida albicans
AUTHOR(S): *Fu Y"**; *Ibrahim AS"**; Fonzi W; Zhou X; Ramos CF; Ghannoum MA (REPRINT)
CORPORATE SOURCE: UNIV CALIF LOS ANGELES,MED CTR, DEPT MED, ST JOHNS CARDIOVASC RES CTR, DIV INFECT DIS/TORRANCE//CA/90509 (REPRINT); UNIV CALIF LOS ANGELES,MED CTR, DEPT MED, ST JOHNS CARDIOVASC RES CTR, DIV INFECT DIS/TORRANCE//CA/90509; GEORGETOWN UNIV,MED CTR, SCH MED, DEPT MICROBIOL & IMMUNOL/WASHINGTON//DC/20007; CASE WESTERN RESERVE UNIV,UNIV CTR MED MYCOL, DEPT DERMATOL/CLEVELAND//OH/44106; CASE WESTERN RESERVE UNIV,MYCOL REFERENCE LAB, DEPT DERMATOL/CLEVELAND//OH/44106; UNIV HOSP CLEVELAND,/CLEVELAND//OH/44106
PUBLICATION TYPE: JOURNAL
PUBLICATION: MICROBIOLOGY-UK, 1997, V143, ,2 (FEB), P331-340
GENUINE ARTICLE#: WH225
PUBLISHER: SOC GENERAL MICROBIOLOGY, MARLBOROUGH HOUSE, BASINGSTOKE RD, SPENCERS WOODS, READING, BERKS, ENGLAND RG7 1AE
ISSN: 1350-0872
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: Extracellular phospholipases are demonstrated virulence factors for a number of pathogenic microbes, The opportunistic pathogen Candida albicans is known to secrete phospholipases and these have been correlated with strain virulence. In an attempt to clone C. albicans genes encoding secreted phospholipases, Saccharomyces cerevisiae was transformed with a C. albicans genomic library and screened for lipolytic activity on egg-yolk agar plates, a traditional screen for phospholipase activity. Two identical clones were obtained which exhibited lipolytic activity. Nucleotide sequence analysis identified an ORF encoding a protein of 351 amino acid residues. Although no extensive homologies were identified, the sequence contained the Gly-X-Ser-X-Gly motif found in prokaryotic and eukaryotic lipases, suggesting a similar activity for the encoded protein. Indeed, culture supernatants from complemented yeast cells contained abundant hydrolytic activity against a triglyceride substrate and had no phospholipase activity. The data suggest that C. albicans. in addition to phospholipases, also has lipases. Southern blot analyses revealed that C. albicans may contain a lipase gene (LIP) family, and that a lipase gene(s) may be present in Candida parapsilosis, Candida tropicalis and Candida krusei, but not in Candida pseudotropicalis, Candida glabrata or S. cerevisiae, Northern blot analyses showed that expression of the LIP1 transcript, the cloned gene which encodes a lipase, was detected only when C. albicans was grown in media containing Tween 80, other Tweens or triglycerides as the sole carbon source, and not in Sabouraud Dextrose Broth or yeast/peptone/dextrose media. Additionally, carbohydrate

supplementation inhibited LIP1 expression, Cloning this gene will allow the construction of LIP1-deficient null mutants which will be critical in determining the role of this gene in candidal virulence.

18/3,AB/15 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06876777 References: 22
TITLE: IN VITRO DETERMINATION OF OPTIMAL ANTIFUNGAL COMBINATIONS AGAINST CRYPTOCOCCUS NEOFORMANS AND CANDIDA ALBICANS
AUTHOR(S): GHANNOUM MA; *FU Y"**; *IBRAHIM AS"**; MORTARA LA; SHAFIQ MC; EDWARDS JE
CORPORATE SOURCE: UNIV CALIF LOS ANGELES,MED CTR,ST JOHN CARDIOVASC RES CTR,DEPT MED,DIV INFECT DIS,BLDG RB2/TORRANCE//CA/90509 (Reprint); UNIV CALIF LOS ANGELES,SCH MED/LOS ANGELES//CA/90024; UNIV CALIF DAVIS,DEPT MOLEC & CELLULAR BIOL/DAVIS//CA/95616
PUBLICATION: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, 1995, V39, N11 (NOV), P 2459-2465
GENUINE ARTICLE#: TD129
ISSN: 0066-4804
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: There is currently no rapid, reliable, and reproducible in vitro technique to describe the growth-inhibitory interactions of antifungal drug combinations over a wide range of drug concentrations, We have developed a microdilution plate assay that was used to determine optimal drug combinations and concentrations of one-, two-, and three-drug regimens of amphotericin B (AmphB), fluconazole (FLU), and 5-fluorocytosine (5FC) for growth inhibition of three isolates each of Cryptococcus neoformans and Candida albicans. These growth inhibition data were then used in a multifactorial design technique to (i) generate contour and surface response plots to aid visual interpretation and (ii) develop mathematical equations describing the growth responses of the fungi to a wide range of antifungal concentrations and ratios. Our data indicated that (i) antifungal drug-drug interactions affecting yeast growth are complex functions of the drugs used in combination, their absolute concentrations, and also their relative (proportional) concentrations; (ii) AmphB-FLU combinations had additive effects against C. albicans over wide concentration ranges for each agent but were indifferent (i.e., were less than additive) in their inhibitory effect on C. neoformans; (iii) other two-drug combinations (FLU-SFC or AmphB: 5FC) had indifferent effects on the growth of both fungi; and (iv) three-drug combinations (AmphB-FLU-5FC) showed an additive inhibitory effect on the growth of both C. albicans and C. neoformans. The finding that no antagonism was observed in combinations employing AmphB and FLU in this in vitro model is of critical importance since it argues against the current theoretical concept, based on the individual drug's mode of action, of antagonism between these two drugs. These microdilution techniques provide a method to determine rational regimens of antifungal agents in multidrug combinations for future testing to correlate in vitro activity with in vivo response. The use of this approach has made the evaluation of complex antifungal drug-drug interactions possible and provided important new information to the evolving field of antifungal drug combination.

18/3,AB/16 (Item 6 from file: 440)

04082827 References: 20
TITLE: SUSCEPTIBILITY TESTING OF CRYPTOCOCCUS-NEOFORMANS - A MICRODILUTION TECHNIQUE
AUTHOR(S): GHANNOUM MA; *IBRAHIM AS"**; *FU Y"**; SHAFIQ MC; EDWARDS JE; CRIDDLE RS
CORPORATE SOURCE: UNIV CALIF LOS ANGELES,MED CTR,DEPT MED,DIV ADULT INFECT DIS/TORRANCE//CA/90509 (Reprint); UNIV CALIF DAVIS,DEPT BIOCHEM & BIOPHYS/DAVIS//CA/95616; UNIV CALIF LOS ANGELES,SCH MED/LOS ANGELES//CA/90024
PUBLICATION: JOURNAL OF CLINICAL MICROBIOLOGY, 1992, V30, N11 (NOV), P 2881-2886
GENUINE ARTICLE#: JU856
ISSN: 0095-1137
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: We studied a series of test conditions in a microtiter system to define the optimal method for determining the susceptibility of Cryptococcus neoformans to antifungal agents. Twenty-one isolates of C neoformans were grown for 24 or 48 h in four chemically defined media: yeast nitrogen base (BYNB 7); RPMI 1640; synthetic amino acid medium-fungal (SAAMF), buffered at pH 7.0 to select the medium that best supported growth of this fastidious yeast; and yeast nitrogen base, pH 5.4 (YNB 5.4). Maximum growth of C. neoformans, at 35-degrees-C, was obtained in YNB 5.4, with the next highest growth levels in BYNB 7, SAAMF, and RPMI. Growth at 24 h was uniformly poor in all media and lacked reproducibility. In contrast, incubation for 48 h gave adequate growth with low standard deviations, and 48 h was selected as the optimal incubation period for this study. Comparison of the relationship between growth kinetics and initial inoculum size for eight cryptococcal isolates showed that 10(4) cells per ml yielded optimal growth in BYNB 7 and YNB 5.4, whereas 10(5) cells per ml was optimal in RPMI and SAAMF. Furthermore, variation of inocula from 10(3) to 10(5) cells per ml showed small but significant inoculum effects in determining MICs of fluconazole, amphotericin B, and flucytosine for C. neoformans. Therefore, 10(4) cells per ml was chosen as the optimal inoculum for susceptibility testing in this study. Mean MICs of fluconazole, amphotericin B, and flucytosine for 21 cryptococcal isolates in RPMI and BYNB 7 were low (for example, fluconazole had mean MICs of 1.2 and 1.3 mug/ml in RPMI and BYNB 7, respectively) and differed significantly from medium to medium. In contrast, the MICs obtained in SAAMF were significantly higher (e.g., fluconazole had a mean MIC of 2.2 mug/ml). Variance in MICs was large with fluconazole and flucytosine but small with amphotericin B, irrespective of the medium used. A microtiter system employing BYNB 7 as the medium, 48 h as the incubation period, and 10(4) cells per ml as the final inoculum is a simple, accurate, and reproducible method for the testing of C. neoformans susceptibility to fluconazole, amphotericin B, and flucytosine.
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07oct02 09:52:56 User219783 Session D1873.2